SURGERY
GYNECOLOGY AND OBSTETRICS
An International Magazine, Published Monthly

VOLUME 76 APRIL, 1943 NUMBER 4

DELAYED CLOSURE OF INCISIONS MADE AT CLOSURE OF COLONIC STOMAS

JOHN deJ. PEMBERTON, M.D., F.A.C.S., and B. MARDEN BLACK, M.D.,
Rochester, Minnesota

FORMERLY it was our custom to manage the incision remaining in the wall of the body after closure of a colonic stoma in essentially the same manner as that in which other incisions of the abdominal parietes are treated. After the opening in the bowel had been closed, the fascia was approximated above the bowel, and the subcutaneous layer and skin were closed snugly. A Penrose drain was so placed that it extended down to the suture line in the bowel. For the most part, such wounds healed satisfactorily, but occasionally rather extensive indolent, subcutaneous abscesses developed. This was true particularly when fecal drainage occurred; in such cases the fecal fistula sometimes failed to close, and subsequent attempts at operative closure were necessary. Infections commonly occur in incisions made for closure, since some degree of contamination by the contents of the bowel at the time of the closure cannot be avoided and since secondary incisions made within a few months thereafter through the scar of a previous incision are less resistant to infection than are primary incisions. Furthermore, when fecal drainage occurs, there is extensive and persistent contamination, and such drainage is not unusual.

From the Division of Surgery of the Mayo Clinic, Rochester, Minnesota.

ANTECEDENT INVESTIGATIONS

About 2 years ago, in an attempt to better our results, particularly in respect to the development of subcutaneous abscesses and fecal fistulas, we adopted the method of delayed closure recently advocated by Coller and Valk for the management of contaminated incisions. These authors reported that the method, known at that time as "delayed primary suture," was first employed extensively and its worth proved by French surgeons in 1918. It was found to be so well suited to military needs, and the results which followed its use were so superior to those which followed primary suture of contaminated war wounds, that it was soon adopted by surgeons in the British and American forces. Since the time of the war of 1914–1918, the method has been widely used for the management of contaminated lacerations (3).

The terms "delayed closure" and "delayed primary suture" mean essentially that the incision is packed open for a time before it is closed. Pool thought that the distinction between "delayed primary suture" and "secondary suture" was a matter of tissue repair rather than of time. A "delayed primary suture" is one in which the edges can be approximated and will unite without the excision of tissue, whereas secondary suture is one in which the epidermis has grown inward and must be ex-

cised for proper union. The distinction, according to Hepburn, was based on the appearance of granulations in the wound, and the time for delayed primary suture usually was considered to be any time before the appearance in the wound of granulations visible to the naked eye. Hepburn proposed, however, that the term be restricted to use in those cases in which suture is undertaken at the time the original packing is removed. The best results were found to follow those closures done within 50 hours after the original operation.

It is not entirely clear why delay of closure of a contaminated incision should result in fewer infected incisions. At the time the method was first used, it was assumed that heavily contaminated wounds were not suitable for suture; as a result, after débridement, smears and cultures were made and the wounds were packed open pending receipt of reports from these examinations. If a large number of organisms of any type were present, or if hemolytic streptococci were present, the incisions were not considered to be suitable for suture and were treated by some other method. As experience increased, however, it became evident that knowledge of the type or types of organisms present in the wound, as judged by the results of smear and culture, could not be relied on as a basis for prediction as to the success or failure of the delayed suture. Meanwhile, it had become apparent that incisions which had been packed open did far better than those that had been sutured primarily. Coller and Valk cultured material obtained from ten wounds contaminated by discharges from the lower bowel. In each case there was a preponderance of the Escherichia coli, with fewer of the Staphylococcus aureus and anhemolytic streptococci. Material from the same wounds was cultured again after the wounds had been packed open for 24 hours. Result of culture was in all cases positive, and the types of organisms found remained the same. Coller and Valk concluded that such a method of packing did not have a bactericidal effect.

Such evidence suggests that packing of a wound open for a period before closure is effected leads to certain changes in the wound which in turn produce an environment less favorable for the persistence of organisms known to be present. On the basis of our own observations, we believe that packing of a wound open for a period, until the surfaces of the wound are relatively dry, prevents to a large extent the collection of serum or blood in the wound. Such collections in already contaminated wounds will almost certainly lead to infection of the wound. In this connection, we may say that Hepburn noted that war wounds that had been packed open in anticipation of delayed primary suture did poorly if a blood clot had collected beneath the pack. Apart from this, the usual explanation (1, 2, 6) for the better results which follow delayed closure is that after coagulation has occurred on the fresh surface of the wound, the open mouths of sectioned lymphatic and blood vessels are plugged and rapid absorption of bacteria cannot occur. DuMortier was able to demonstrate experimentally that with the passage of time, sutured incisions became increasingly resistant to infection and that when infections did occur they were less extensive. He made incisions through the skin, subcutaneous tissues and muscular layer of the abdominal walls of guinea-pigs and swabbed gently, after varying intervals of time, the sutured incisions with a fresh virulent culture of what he called the "Staphylococcus aureus hemolyticus." He found that there was a well defined period of about 6 hours during which resistance of the tissue to bacterial invasion was minimal. During this period the bacteria caused not only local suppuration, but also invaded the surrounding tissues and initiated spreading infections. When, on the other hand, the bacteria were swabbed on the sutured incisions 12 hours after operations, most of the incisions became infected, but the infections remained localized. From this time (that is, 12 hours) onward, the percentage and severity of infections steadily decreased until, 5 days after operation, it was no longer possible to infect the wounds by swabbing on the cultures.

The optimal interval at which the wound should be packed open is not known with certainty. On the basis of experience in the treatment of war wounds, the best results follow closure carried out within 50 hours of the operation. Coller and Valk believed that there is little to be gained by delay of closure for more

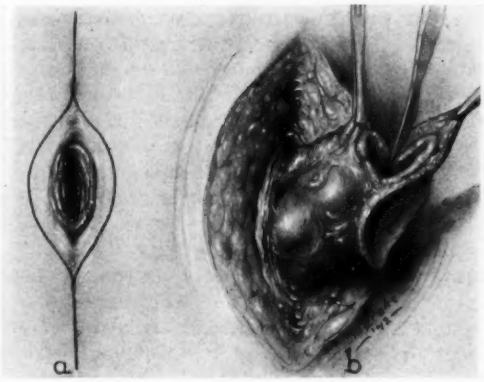


Fig. 1.

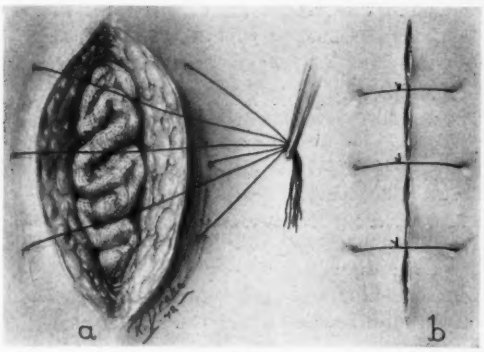


Fig. 3.

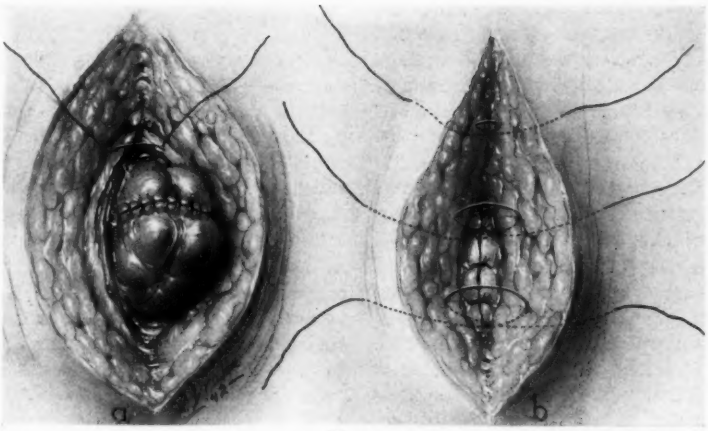


Fig. 2.

Fig. 1. a, Incision made in the skin through the scar of the original incision made in performance of colostomy: the incision is carried around the opening in the bowel, so that a small margin of skin remains; b, technique of dissection of bowel from the body wall. The cuff of scar tissue and skin around the opening in the colon is partially excised.

Fig. 2. a, The opening in the colon is closed, and the fascial layer is partially closed; complete closure of this layer above the bowel restores the strength of the body wall; b, the fascia is closed completely above the bowel; silkworm gut sutures are in place.

Fig. 3. a, The iodoform gauze pack is in place, holding the skin and subcutaneous tissues open, and the ends of the silkworm gut sutures are held in a hemostat; b, appearance of final closure after the pack has been removed and the silkworm gut sutures have been tied.

than 24 hours. We have waited 48 hours, however, before closure of incisions in the belief that after such an interval the patient will have had time to recover somewhat from the operation and that surfaces of the wound appear drier at end of 48 hours than at end of 24.

TECHNIQUE

The technique of our present method of closure of colonic stomas differs from our former method of closure only in the treatment of the skin and subcutaneous tissues. It should be emphasized that before closure is attempted there must be adequate room to permit the bowel to be closed without encroaching on its lumen, and that the spur must have been adequately destroyed. An incision which is sufficiently long to provide adequate exposure is made through the scar of the former incision and is carried around the opening in the bowel.

TABLE I. — COMPARISON: RESULTS AFTER DELAYED AND PRIMARY CLOSURE OF INCISIONS MADE AT CLOSURE OF COLONIC STOMAS

Cases	Type of closure Primary	Delayed
Without fecal drainage	29	33
With fecal drainage (spontaneous)	17	7
With fecal drainage (closure around clamp)	1	7
Total	47	47
Closure failed	7*	1†

*One failure due possibly to inadequately destroyed spur
†Due clearly to inadequately destroyed spur

The bowel is freed up from the body wall and the fascia is cleaned of fat and scar tissue sufficiently to provide a definite layer which subsequently can be approximated to restore the strength of the body wall. Generally, this can be done without making an opening into the peritoneal cavity, but, if a small opening is made inadvertently through the peritoneum, little harm will be done, since it can be closed promptly before opportunity for soiling arises. The skin and scar tissue around the opening in the bowel are excised (Fig. 1, a and b). The opening in the bowel is closed transversely to the long axis of the bowel with two rows of continuous surgical gut sutures (Fig. 2, a and b). The previously freed-up muscular and fascial layer is approximated above the sutured bowel with interrupted surgical gut sutures. Silkworm gut sutures are then placed as is shown in Figure 2, b. A generous "bite" is taken through the skin on one edge of the wound, the needle is reversed to pick up the fascia and is then continued in the original direction through the skin of the other edge of the wound. Usually, three such sutures are sufficient. The skin and subcutaneous tissues are packed open widely with iodoform gauze, and silkworm gut sutures are held loosely in a hemostat (Fig. 3, a). The wound is then dressed. As a rule, dressings do not need to be changed before they are removed for closure of the wound. After 48 hours, the packing is removed and the previously placed silkworm gut sutures are tied sufficiently tightly to approximate the edges of the skin (Fig. 3, b). Some degree of edema of the edges of the incision will have occurred by this time, and in our first few cases, after the edema had subsided, approximation of the edges of the wound was poor because the silkworm gut sutures had been tied too loosely. This was easily corrected in subsequent closures.

After this method of delayed closure had been employed successfully for several months, it was thought that local use of one of the sulfonamide drugs might help in freeing the wound of some of the contaminating organisms. At first 5 grams of sulfanilamide was placed in the wound just before the packing, but more recently the same amount of sulfathiazole has been used. We have not observed any difference in the healing of the wounds regardless of whether a sulfonamide drug was or was not used, but we are continuing to use it on theoretic grounds.

RESULTS

To evaluate our results obtained after the described change of technique, records concerning the last 47 primary closures and the first 47 delayed closures carried out on the same service by one of us (Pemberton) were reviewed. The operations in each group represented a consecutive series, but only typical operations of each type were included. Early in the investigation it became evident that the only significant differences between the two types of closure, in so far as healing is concerned, appeared in cases of fecal drainage. In cases in which there was no fecal drainage, both types of wounds healed solidly, and the time of healing, as judged by the duration of drainage, was the same. Twenty-nine primary closures in which there was no fecal drainage were entirely healed after an average time of 20.3 days and 33 comparable delayed closures were healed after an average time of 20.5 days (Table I). Fluid which drained from the wounds in which delayed closure was carried out was serous, and came from the small regions of granulation tissue which resulted from the comparatively loose closure employed, as previously described. Fluid which drained in the cases in which primary closure was carried out originated from the site of the drain itself, and usually became seropurulent before complete healing occurred.

Spontaneous fecal drainage and primary closure. Spontaneous fecal drainage was far more likely to occur after primary closure than after delayed closure, and extensive infections were

the rule after primary closure when this particular complication developed. Of the 46 primary closures in which the bowel had been closed completely at the primary operation, spontaneous fecal drainage developed in 17. For the most part, the incisions became extensively undermined by abscesses containing pus and feces. Multiple drainage points appeared along the thinned-out sutured incision, and it was necessary in some cases to open the incision somewhat to provide for more adequate drainage. Fever and malaise developed in some patients, and prolonged hospitalization with much local treatment in the form of hot compresses and irrigations was required. In 10 of the 17 cases of fecal drainage, drainage finally stopped after an average interval of 30.4 days. In 7 of this same group of 17 cases fecal drainage did not stop, and, when the infection finally subsided, a fecal fistula remained that required subsequent operative closure. In only one case was failure of the closure possibly due to an inadequately destroyed spur. Of considerable importance in this connection is the fact that after such extensive infections, the amount of scar tissue in the body wall is increased and subsequent attempts at closure are more difficult technically and more likely to fail.

Spontaneous fecal drainage and delayed closure. As compared to the 17 cases of spontaneous fecal drainage, included among the aforementioned 46 cases of primary closure in which the bowel had been closed completely at the primary operation, there were only 7 cases of spontaneous fecal drainage in the group of 40 cases of delayed closure in which the bowel was closed completely. The incisions in the latter cases differed markedly from those in the group in which primary closure had been done, in that undermining was rarely seen (1 case only) and there were no extensive abscesses. The edges of the incision remained firm, and fecal and purulent material usually came from a single region. Generally, there was no fever or malaise, and the patients were able to leave the hospital after a shorter interval. The only local treatment necessary was maintenance of cleanliness in the region by the use of irrigations and by changes of dressing.

Fecal drainage and closure about a clamp. It is possible, occasionally, to apply a crushing clamp to destroy completely a small spur at the time closure is done. In such cases the clamp is left protruding from the incision, and the opening in the bowel cannot be closed completely. Fecal drainage occurs along the shank of the clamp, and in such cases persistent fecal contamination is present in the incision from the time of the operation onward. Our rather distressing experience with such closures around a clamp when the wound had been closed primarily led us to employ this method only rarely. In only 1 case in the last 47 cases in which primary closure was carried out was true primary closure around a clamp attempted. The incision healed satisfactorily after 28 days. Healing after delayed closure in cases in which spontaneous fecal drainage occurred was so satisfactory that more closures around a clamp were attempted, and in the series of 47 cases of delayed closure, closure around a clamp was done seven times. Healing of these incisions did not differ from the healing of those incisions in which spontaneous fecal drainage developed. In 11 of the 14 cases in which delayed closure was carried out and in which fecal drainage occurred, both spontaneously and after closure around a clamp, healing of the incision was complete after an average time of 26.3 days. Two incisions were still draining after 31 and 45 days, respectively, but both fecal fistulas which were present ultimately closed without need for additional surgical treatment. In only 1 of the 47 cases in which delayed closure was employed did the wound fail to heal, and it was in this case that a persistent fecal fistula remained. Subsequently, the fistula was explored surgically, and the failure was found to be due clearly to a large remaining spur. A crushing clamp was applied to this spur and the mucosa was freed up from the skin. Spontaneous closure ultimately resulted.

CONCLUSIONS

The incision remaining in the body wall after closure of a colonic stoma generally is contaminated by bacteria from the open bowel. Delayed closure of such incisions is definitely superior to primary closure of them. When delayed closure is employed, the incisions become infected less frequently and the infections are less extensive and require less treatment than

when primary closure is carried out. Fewer spontaneous fecal fistulas occur, and there is less chance for closure to fail when delayed closure is used than when primary closure is used. Closure around clamps can be attempted with greater chance of success when closure of the incision is delayed than is possible when closure is primary. Our satisfactory experience with delayed closure of colonic stomas is in accord with the experience of others in the management of other types of contaminated wounds.

REFERENCES

1. COLLER, F. A., and VALK, W. L. Ann. Surg., 1940, 112: 256–262.
2. DUMORTIER, J. J. Surg. Gyn. Obst., 1933, 56: 762–766.
3. GAMBLE, H. A. Discussion. Ann. Surg., 1940, 112: 264–265.
4. HEPBURN, H. H. Brit. M. J., 1919, 1: 181–183.
5. POOL, E. H. J. Am. M. Ass., 1919, 73: 383–387.
6. WELCH, W. H. In Dennis, F. S. System of Surgery. Vol. 1, p. 279. Philadelphia: Lea Bros. & Co., 1895.

PANLARYNGECTOMY FOR ADVANCED CARCINOMA OF THE LARYNX

ALEXANDER BRUNSCHWIG, M.D., F.A.C.S , Chicago, Illinois

PATIENTS with advanced extrinsic laryngeal cancer present a distressing situation for which there is practically no hope for cure and for which conservtive palliative procedures are usually of little avail. Pain is an outstanding complaint, difficulty with respiration is more or less constant unless there is a tracheotomy tube in place, and the sanguinopurulent discharges add to the general discomfort.

In a series of 5 patients with advanced extrinsic laryngeal carcinoma in which irradiation therapy had been carried out but failed to control the growth, the writer performed a radical surgical excision encompassing the gross limits of the tumor. While "cure" was not anticipated, the clinical course in the limited series was such as to have justified the performance of this operation as a palliative measure, there having been no clinical or roentgenological evidence of metastases beyond the cervical region at operation.

TECHNIQUE OF OPERATION

Operation is not attempted if the tumor-mass-larynx is "frozen" to the vertebral column.

Avertin, avertin and local anesthesia, or avertin and local and intratracheal ether anesthesia are the types of anesthesia used (the anesthetist scrubbing up with the operative team).

1. A T-incision is made with the horizontal segment just above and parallel to the hyoid bone (Fig. 1).

2. The skin and platysma flaps are elevated to the right and left.

3. The trachea below the isthmus of the thyroid gland is isolated and transected; the lower opened segment is brought into the lower angle of the wound and the tracheotomy tube is inserted. If the latter has been inserted previously the transection of the trachea is carried out above the tracheotomy site. A gauze plug is inserted into the upper segment of the transected trachea to prevent constant dripping of the secretions.

4. The infrahyoid group of muscles in the lower neck is transected.

5. First on one side the cervical chain of nodes are dissected *en masse* upward. One or the other jugular vein if closely associated with involved nodes is doubly ligated and transected in the lower neck, the upper segment being retracted upward. If metastatic nodes are likewise adherent to the common carotid artery, the latter may also be doubly ligated and transected low in the neck. Prior to this step a rubber covered clamp is applied to the common carotid in the base of the neck,

From the Department of Surgery of the University of Chicago.

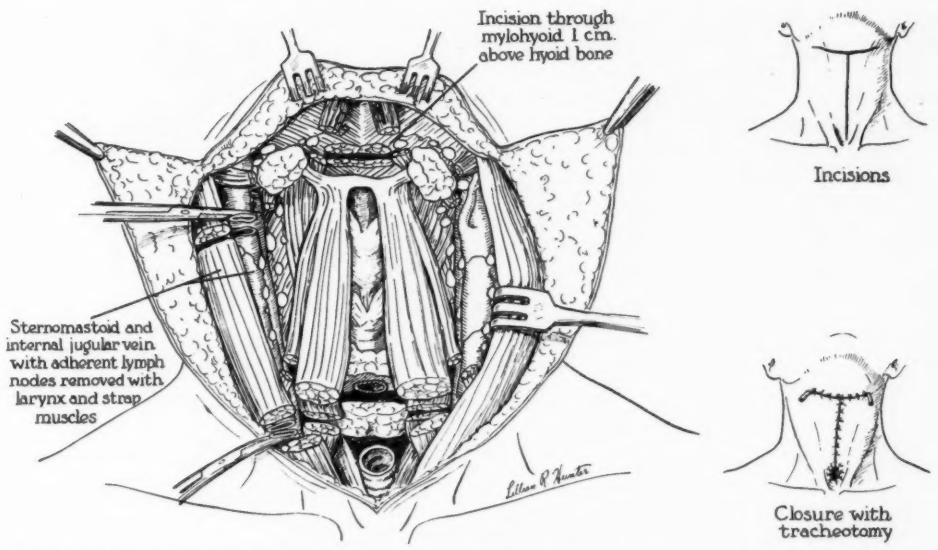

Incision through mylohyoid 1 cm. above hyoid bone
Sternomastoid and internal jugular vein with adherent lymph nodes removed with larynx and strap muscles
Incisions
Closure with tracheotomy

Fig. 1. Schematic illustration of panlaryngectomy. The strap muscles are transected low in the neck; both bellies of the digastrics are cut; the submaxillary glands and nodes are dissected free *en masse* and reflected downward and toward the midline; the mylohyoid muscle is cut through into the pharynx. When a jugular vein and adherent carcinomatous nodes are to be excised with the larynx and attached muscles, the vein is transected low in the neck and as high in the neck as possible. To obtain a block excision, the sternomastoid is also freed by transection near its insertion and near its origin, and removed *en masse* with the other structures excised. The trachea is divided below the isthmus of the thyroid and the lower end is brought up to level of skin. The upper half of the thyroid, or the upper portions of both poles, adherent to the trachea is removed. At the completion of the operation the trachea is sutured to the skin with interrupted silk sutures; small rubber drains are inserted into each extremity of the horizontal portion of the incision, and stab wounds may also be made in the lower portions of the neck on each side for drainage.

and pulse, blood pressure, and respirations are observed for 10 minutes. If there are significant disturbances of the latter, the clamp is removed, and the common carotid artery must be left *in situ*. When the jugular vein or carotid or both are to be removed, resection of the sternomastoid muscle on that side is likewise indicated (Fig. 4).

6. If necessary the upper poles, or upper half of the thyroid gland, is freed from the lower portions and elevated with the tumor mass to be resected.

7. The tumor-mass-larynx is then freed by wide sharp dissection upward to the upper portions of the neck. The submaxillary glands and adjacent lymph nodes are freed first in the lateral portions of the submaxillary triangles in such a manner that they will be elevated medially and excised *en masse* with the larynx. The tissues in the submaxillary triangles should not be excised as separate masses.

8. A transverse incision is then made through the muscles about 1 or 2 centimeters above the hyoid bone. This incision is carried through the base of the tongue into the pharynx.

9. The tumor-mass-larynx is then freed by widely cutting away the larynx from the hypopharynx. This may or may not entail removal of the epiglottis.

There remains only a strip of hypopharyngeal and upper cervical esophageal mucosa posteriorly. This varies from 1.5 to 2.5 centimeters in width depending upon the extent of laryngeal resection.

10. The hypopharyngeal and upper cervical esophageal mucosa are sutured as a tube over a Levine tube inserted through the nose into the esophagus by interrupted catgut sutures.

Fig. 2.

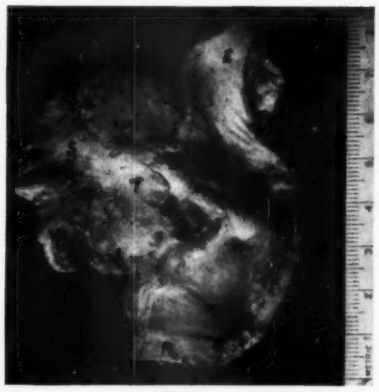


Fig. 3.

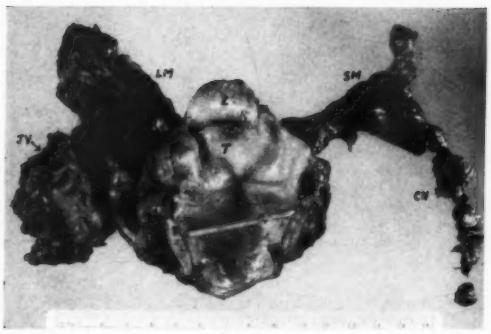


Fig. 4.

Fig. 5.

Fig. 6.

Fig. 2. Case 1, No. 206882. Photograph of cervical region 40 months after panlaryngectomy showing large tracheotomy opening, and sulcus due to absence of most of soft tissues in midportion of neck. The patient is normally active 4 years after operation and presents no evidence of recurrences. A tracheotomy tube is not worn. He has gained 50 pounds in weight since operation.

Fig. 3. Case 1, No. 206882. Bisected surgical specimen removed by panlaryngectomy showing, *T*, large squamous cell carcinoma of larynx fungating anteriorly through skin of neck producing large sinus, *S*. Epiglottis, *E*, transected trachea, *R*.

Fig. 4. Case 4, No. 243693. Surgical specimen removed by panlaryngectomy: *T*, carcinoma of larynx; *E*, epiglottis; *S M*, right submaxillary gland and lymph nodes; *C N*, right chain of cervical lymph nodes with metastatic carcinoma; *L M*, left sternomastoid muscle; *J V*, left internal jugular vein surrounded by adherent metastatic cervical lymph nodes.

Fig. 5. Case 4, No. 243693. Appearance of patient 1 week after operation. Secondary hemorrhage several hours after operation necessitated separation of wound and packing it with gauze. *R*, tracheotomy opening; *L*, nasal tube in esophagus, the anterior wall of which has been resected; bullous edema of esophagus is apparent.

Fig. 6. Case 4, No. 243693. Appearance of neck 8 months after operation showing large sinus the posterior wall of which is composed of hypopharyngeal and esophageal mucosa. The tracheotomy is seen in the lower angle of the wound and the patient did not wear a tube most of the time. He nourished himself by insertion of a Levine tube into the sinus at intervals. He was ambulatory and wore a small piece of gauze over the anterior neck when going outside.

Soft rubber drains are inserted into each side of the large defects which are present in the neck.

11. The transected lower segment of trachea is attached to the skin by interrupted silk sutures and a tracheotomy tube is inserted in the usual manner.

Postoperative course. Secondary infection invariably results in a partial or wide reopening of the wound (Fig. 5). However, the pain and distress present before operation are alleviated and if survival obtains the patients are comfortable and are much more content for a period than they were prior to the operation.

TABLE I.—SUMMARY OF 5 CASES

Patient Age Case No.	History	Present status	Operation	Postoperative course
I. W. M. ♂ 55 yr. (206882)	Carcinoma of larynx demonstrated by biopsy, October, 1938—neoplasm involving left cord and quite large. History of hoarseness for 2 years. X-ray therapy 4300 r surface dose in air, October–November, 1938. Immediate improvement. Abscess developed in neck over larynx, February, 1939, drained. Sinus persisted, hoarseness aggravated	Extensive firm induration palpable about larynx with sinus in midline from which neoplastic granulations protrude	Panlaryngectomy 4–10–39 with excision of skin on anterior aspect of neck to include sinus. Epiglottis removed (Fig. 3)	Satisfactory convalescence. Partial separation of wound but subsequent healing. Patient gained 50 pounds in weight since operation and has been doing physical labor. Satisfactory nutrition by mouth with liquid and semisolid foods. Survival since operation: 4 years. No evidence of neoplasm (Fig. 1)
II. T. L. ♂ 47 yr. (71533)	Carcinoma, base of epiglottis diagnosed by biopsy 8–8–38. X-ray therapy August–September, 1938, 6655 r to two portals. Improvement. Recurrence with 2275 r x-ray in June, 1939. Tracheotomy, November, 1939	Marked woody induration about larynx. Carcinomatous mass involving larynx, hypopharynx and infiltrating surrounding tissues	Panlaryngectomy, left jugular vein and sternomastoid also resected. Epiglottis removed *in toto* with larynx	Postoperative course satisfactory. Operative wound partially separated but by end of 36th day postoperative could nourish himself by mouth with soft and liquid food. On 40th day while walking down hall in hospital sudden massive fatal hemorrhage occurred. Necropsy revealed this to have come from area in upper left common carotid artery invaded by tumor
III. A. M. ♂ 63 yr. (239785)	Resection of "papilloma" of vocal cord and tracheotomy 9–19–39. X-ray therapy Dec., 1939, to Jan., 1940, 3100 r	Large perilaryngeal tumor mass. Tracheotomy tube in place. Severe pain in larynx. Dysphasia	Panlaryngectomy including resection of epiglottis 4–29–40. Convalescence complicated by bronchopneumonia	Relieved of severe pain. Partial separation of operative wound. Gained 14 pounds in weight from September to December, 1940. Neoplasm recurred in margins of wound. These were fulgurated to retard growth. By April, 1941, cervical tumor mass had become quite large but there was no pain. Died at home April 20, 1941. No necropsy. Survived operation 1 year
IV. A. Y. ♂ 57 yr. (243693)	X-ray therapy to larynx (dose unknown in September, 1939) Some pain in larynx and some dysphagia. Progressive increase in hoarseness	Tumor mass involving larynx and palpable firm enlarged cervical lymph nodes, bilateral	Panlaryngectomy 6–25–40 including resection of epiglottis and left jugular vein	Hemorrhage into upper portion of operative wound on second day necessitated its opening and packing with gauze. Subsequent convalescence satisfactory. Evidence of local recurrences November, 1940. Excision of local recurrences on several occasions. Plastic closure of defect in neck by skin flap from shoulder. Radium implantations about individual recurrent masses resulted in their temporary shrinkage. Recurrences finally out of control and patient died of hemorrhage 1–2–42 from large infected neoplastic mass in neck. He had survived 19 months following the operation
V. D. S. ♂ 50 yr. (138709)	Biopsy of lesion in larynx 10–22–35 revealed carcinoma. X-ray therapy October–November, 1935, to larynx, total dose 4240 r. This was followed by regression of lesion. Hoarseness did not improve. Tracheotomy in July, 1941, because of acute respiratory difficulty. Developed tracheoesophageal fistula necessitating gastrostomy 11–1–41	Firm swelling palpable about larynx. Fungating tumor mass replacing larynx. Metastatic nodes palpable in both upper cervical regions. Intense pain in neck radiating to head	Panlaryngectomy 11–13–41. Jugular veins not resected	Convalescence satisfactory. Wound separation. Patient fairly comfortable and previous pain relieved. Small nodules of recurrent carcinoma in margins of wound observed January 4, 1942. These and subsequent recurrences excised. Period of weight gain December, 1941, to February, 1942. Frequent small hemorrhages March and April, 1942. Died May 19, 1942, from massive hemorrhage. Necropsy not performed. Survived operation 6 months

Although a large esophageal sinus and tracheotomy may be present in the neck, the patients learn to tube-feed themselves, are ambulatory, and learn to get along quite well wearing a relatively small gauze dressing over the anterior aspect of the neck. Frequently the tracheotomy tube is dispensed with (Fig. 6).

The question of speech does not present a serious problem since speech can hardly be recognized to exist prior to the operation in view of the extensive lesion present.

The cases in which the procedure was performed are briefly summarized in Table I. In each instance the patient appeared quite ill prior to operation. All 5 patients subjected to panlaryngectomy experienced a period of increased comfort after operation and there were no immediate postoperative deaths. In Case 1, patient lived 48 months (is still clinically well, neck healed, normally active); in Case 2, patient lived 36 days and died from sudden massive hemorrhage; in Case 3 patient lived 12 months; in Case 4, 19 months,

and in Case 5, 6 months; these latter 3 all died with recurrence.

Nutrition. Because of the wide resection of the anterior wall of the cervical esophagus tube feedings are necessary. Levine tubes are passed into the esophagus through the nose or directly into the esophageal sinus in the neck. Maintenance or even gain in weight was possible by suitable "tube diets." In Case 1 complete closure of the neck wound was possible. In Case 5 there was also a gastrostomy and while it might appear that a patient with both a tracheotomy and gastrostomy might represent an individual who "may just as well be dead," his existence during most of the postoperative period was far more comfortable than it was prior to operation when he had a very painful laryngeal neoplasm and tracheoesophageal fistula. During most of the period of survival he was ambulatory and even did light physical work at times. In this connection the question of prolongation of life in patients with advanced carcinoma presents itself. It is the surgeon's duty to employ, with judgment, all measures which may prolong life in patients with advanced carcinoma provided it may be reasonably expected that the added period of existence will be spent in greater comfort than that prior to the operation and that the patient will not be made to lead a purely "vegetative" existence. Another justification for attempting resection of "inoperable" carcinomas in patients in whom there is no evidence of distant spread is the fact that it is not very uncommon to observe unusually prolonged survivals with comfort in patients who have had malignant neoplasms resected but in whom conditions were such at the time of operation that the surgeon had every reason to be very pessimistic as to the subsequent duration of life.

SUMMARY

Panlaryngectomy was performed to remove advanced extrinsic carcinoma of the larynx in 5 patients who had previously received x-ray therapy which had not eradicated the neoplasm. The palliative results observed justify the procedure carried out in this group of patients.

THE EFFECT OF SECTIONING VARIOUS AUTONOMIC NERVES UPON THE RATE OF EMPTYING OF THE BILIARY TRACT IN THE CAT

FRANK E. JOHNSON, M.S , and EDWARD A. BOYDEN, Ph.D. (Med.Sc.), Minneapolis, Minn.

NOTWITHSTANDING the intensified interest and the great progress made in the field of biliary physiology during the last two decades, the 1925 dictum of A. J. Carlson still stands: "As regards the extrinsic nerve control of the contraction of the gall bladder and the musculature of the bile passages, and particularly the sphincter of Oddi, there are few fields in experimental physiology in which so much serious work has been done with so few conclusive results."

In partial explanation of this situation it may be noted that only comparatively recently has it been realized that the mechanism of evacuation may be primarily hormonal; so that the problem is not whether nerves cause or prevent emptying but to what degree, and how the autonomic nervous system modifies the activity of the biliary tract. Second, there is a surprising paucity of detailed information about the nerve supply of the biliary tract. Third, the experiments have been mostly acute experiments, "frighting Nature out of her usual byas" (to quote Robert Hooke), and thus not permitting analysis of natural functions under conditions approaching those to be found in the intact animal.

In the attempt to meet some of these deficiencies, Schulze and Boyden (1943) investigated the innervation of the biliary tract in the cat, an animal in which reflex inhibition of the gall bladder can be induced by faradic stimulation of the gut from stomach to cecum (Birch and Boyden, 1930). By employing a modification of the Wharton-Siehler technique of stretching a given nerve field on a flat surface, staining it *in toto* with Ehrlich's hematoxylin, decolorizing it, and dissecting the nerves in glycerine with the aid of a binocular microscope, two independent pathways to the choledochoduodenal junction were discovered—a *gastroduodenal plexus*, lying between the artery of that name and the common bile duct, and a discrete *gastroduodenal nerve* which descends from the hepatic plexus a little to the left of the gastroduodenal artery (Fig. 1). It was the finding of this nerve, whose components could be traced to the right vagus and both celiac ganglia, that suggested to the senior author the possibility of interrupting the pathways to the choledochoduodenal junction and of ascertaining how this affected the rate of emptying of the biliary tract in the unanesthetized and postoperatively recovered animal.

From the Department of Anatomy, University of Minnesota.
Prepared for presentation before the Forum on Fundamental Surgical Problems, 1942 Clinical Congress of the American College of Surgeons, which was cancelled because of the war.

EXPERIMENTAL AND OPERATIVE PROCEDURES

The first experiments were designed to interrupt the specific pathways to the choledochoduodenal junction—namely, the gastroduodenal nerve and plexus.

A cat, which had had no food for at least 12 hours previous to the operation, was brought to surgical anesthesia with ether and the body cavity was then entered through a midventral incision. The stomach was retracted inferiorly to expose the lesser omentum. The omental bursa was entered by passing through the gastrohepatic ligament. Then the hepatic artery was picked up in the right gastropancreatic fold and the gastroduodenal nerve located just caudad to the hepatic artery (Fig. 1). The nerve was followed to the right as far as the origin of the gastroduodenal artery to be certain that it had received all its components. At this point in its course, as it lay just to the left of the gastroduodenal artery, it was severed or doubly ligated. A complicating factor here was found to be a large and quite constant lymph node

(one of the hepatic chain) situated in the angle formed by the hepatic and gastroduodenal arteries. This node lay superficial to the gastroduodenal nerve, often completely concealing it, and had to be reflected. Next the tissue to the right of the gastroduodenal artery was isolated down to the portal vein, and the anterior surface of this vein was stripped clean of loose connective tissue and nerve plexus. The posterior and medial wall of the common bile duct at the level of the origin of the gastroduodenal artery were also stripped, care being taken not to traumatize the common bile duct. Two ligatures were passed through the opening thus made and tied tightly, so that the gastroduodenal artery and its surrounding gastroduodenal plexus were doubly ligated. In view of the thinness of the supporting tissues, this procedure was considered to be adequate to prevent impulses from passing to the choledochoduodenal junction over these specific nerves. Incidentally, ligation of the artery did not produce any visible deterioration in the duodenum. This was also the experience of Bergh (personal communication) who found that any two of the arteries to the stomach could be ligated without producing gangrene.

In the second set of experiments the dorsal (s. right) vagus nerve was severed at the point where it emerges from the diaphragm with the primary object of interrupting its main contribution to the gastroduodenal nerve. Incidentally, this also eliminated fibers supplying the gall bladder and stomach. Subsequently, in other cats, as a control experiment, the ventral (s. left) vagus was severed at the same level, the right vagus being left intact.

In the third series of operations, the thoracolumbar autonomic supply to the biliary duct system was eliminated. For this procedure, medium-sized to small cats were found to be the most suitable. The body cavity was again entered through a midventral incision. The greater and lesser splanchnic nerves were picked up and sectioned in their course from the diaphragm to the celiac ganglia. On the left side the ganglion lies just median to the left adrenal gland and spread upon the superior mesenteric and celiac arteries near their origin from the aorta. On the right side the ganglion usually lies deep to the upper pole of the right adrenal gland.

In variations of this procedure, in which the lumbar sympathetic trunk or lumbar roots of the celiac ganglion were picked up as they lay in the crevice between the crura of the diaphragm and the psoas muscles, it was found advisable to tear the parietal peritoneum and renal fascia above the kidney and to retract this organ inferiorly, in order to make the operative field adequate. Also, to expose the desired nerves (especially the lumbar roots of the celiac ganglia) for sectioning, it was usually necessary to doubly ligate and sever the large adrenolumbar vein. The right side presented the most difficulty for two reasons: first, the right celiac ganglion was often concealed by the adrenal gland or the inferior vena cava, or by mesenteries running to the vein from the liver; second, the attachment of the caudate process of the liver so near to the ganglion made it virtually impossible to expose this nerve without traumatizing the liver. However, the resulting hemorrhage was readily stopped by packing.

In other experiments, nerves were sectioned in various combinations to be described later.

After the nerves had been severed in each animal, an insulated electrode previously prepared according to the method of Birch and Boyden (1930), was sewed to the greater curvature of the cecum. This consisted of the divided ends of two enamelled wires enclosed and tied into a small-gauge, flexible rubber tube. (Note silhouette of wires in Fig. 2.) At the end containing the electrode, the tube had been split lengthwise for a short distance and its upper half discarded. At the time of operation, the other half, in which the electrode rested, was inverted and sewed by its edges to the cecum. The undivided end of the tube was then brought out through the laparotomy wound, the wires connected to an induction coil, and the apparatus tested on the operating table. Closing of the circuit produced a ring-shaped spasm of the cecum at the level of the electrode.

The last step consisted of rendering the gall bladder opaque to the x-ray. According to the method of Whitaker (1926), an avascular spot on the fundus was perforated with a surgical

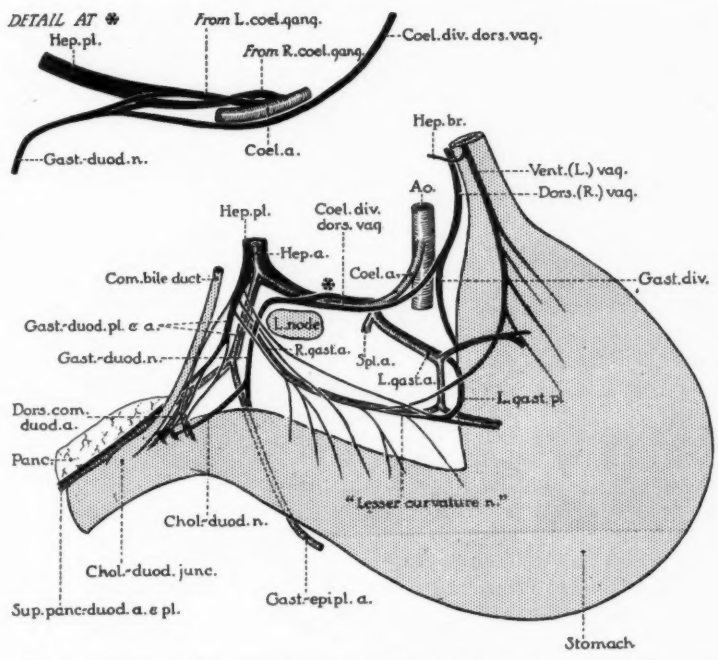


Fig. 1. Diagram of the innervation of the biliary tract in the cat (after Schulze and Boyden, 1943). In the region of the bile duct the structures have been drawn as if somewhat spread apart, in order to display them better.

needle, the bile milked from the gall bladder, and the latter filled to its original size with lipiodol—an iodized vegetable oil.

The body cavity was then closed and the rubber tube with its contained wires led to the outside through the incision. By means of this arrangement, it was possible to stimulate the cecum in the unanesthetized animal some 15 hours after operation and to see how section of various nerves affected the reflex from gut tract to gall bladder and whether this involved the sphincter.

Immediately after the operation, two roentgenograms were taken to determine the condition of the gall bladder. The next morning, 12 to 16 hours after the operation, when the cat had fully recovered and was moving about, another picture was taken to make certain that the gall bladder had not emptied during the night. The cats were then fed a meal of two egg-yolks and milk by gavage. Strangely, this meal usually soothed and pacified the cats so that soon after being placed on the x-ray table and petted, they began to purr.

Immediately after the meal, pictures were taken at short intervals to determine when the gall bladder came into tonus and when it first started to empty. When it was established that the column of lipiodol had reached the cystic duct a picture was taken, then a faradic current (with induction coil set at 4 cm.) was sent into the cecum for 10 seconds. Forty-five seconds after the first picture a second was taken. Then another current was sent in and 45 seconds after the second current, or a minute and a half after the first, a third picture was taken. These were then studied to determine the presence or absence of the inhibitory reflex.

As a control experiment, the wound and skin of the belly wall of the same cats in which the inhibitory reflex had been demonstrated, were pinched with forceps, or faradically stimulated, and x-ray pictures were

TABLE I.—NORMAL RATE OF EMPTYING OF GALL BLADDER IN 12 CATS

Cat	Initial tonus min.	Oil enters cystic duct min.	Rate of evacuation of gall bladder (min. after food)		
			⅓ empty, min.	⅔ empty, min.	Empty, min.
A — Group 1					
18	4−	6−	40+	44−	44
21	0−	0−	13*	23−	90
20	4−	4	11*	18	93
16	13−	13	19*	23	151
24	9+	9−	20*	48*	212
11	3	25	35*	48−	48+
28	2−	2−	28	58	251+
Av.	6)35(6′−	6)59(10′−	7)166(24′	7)262(37′−	7)889(127′+
B — Group 2					
27	—	27	75	131	322+
9	36	70	234	317	464
14	—	—	132*	202	512+
15	6−	30−	140*	184	519
17	8	14	91	156*	521
Av.	3)50(17 35	4)141(37 59	5)672(134′ 166	5)990(198 262	5)2338(468 889
Av. (A & B)	9)85(9′	10)200(20′	12)838(70′	12)1252(104′	12)3227(269′

Data reconstructed from tables and figures of DuBois and Hunt, 1932.
*Estimated by interpolation.

taken at the same time intervals as before (viz., Fig. 2, second row), thus to eliminate the possibility that certain results could be explained on the basis of a cutaneovisceral reflex or that the change in shape of the gall bladder had been due to mechanical pressure caused by the struggling of the animal in response to pain. Also, the induction coil was buzzed for 2 seconds without sending the current to the cecum to determine the presence of a conditioned reflex.

When the gall bladder was empty or nearly so, the cat was sacrificed, an autopsy was done, and drawings were made to record exactly which nerves had been cut and which remained.

Records were kept of the emptying time of the gall bladder and compared with the data of DuBois and Hunt (1932) who established the rate of evacuation of the gall bladder in normal cats following a meal of egg-yolk.

OBSERVATIONS

1. The normal rate of emptying in the cat. The only adequate information regarding the normal rate of emptying of the gall bladder in mammals other than man is that supplied by DuBois and Hunt (1932) for the cat and the opossum. This was obtained by opening the body cavity, expressing the bile through a small aperture in the fundus, and refilling the gall bladder with an iodized oil opaque to the x-ray. Some 12 to 15 hours later, when the animals were in apparently good condition—walking around and purring—they were fed (by gavage) a standard meal of three to four egg-yolks and 30 to 50 cubic centimeters of cream; then x-rayed at frequent intervals until the gall bladder was completely empty.

In addition to tables, the authors published a series of silhouettes of each gall bladder. By using these figures, a table has been reconstructed which supplies additional information and makes possible a direct comparison with the data presented in this thesis.

A study of Table I emphasizes the findings of DuBois and Hunt, namely, that the 12 cats fell into two series: *A*, a group of 7 in which the gall bladder emptied approximately two-

thirds of its contents in an average of less than 40 minutes after eating; and *B*, a group of 5 animals in which the principal period of discharge was spread over a period of some 3 hours, in such a way that the two-thirds mark was not reached until an average time had elapsed of over 198 minutes after food. No experimental analysis of these variations was attempted, but the present experiments suggest that in addition to the varying reaction of the animals to the shock of operation, the varying balance of sympathetic and parasympathetic control may have been a factor.

In comparing these figures with the data presented in this thesis, the average figures for all 12 animals of DuBois and Hunt have been used.

In concluding this section, it should be stated that the relative size of the gall bladder at different intervals was estimated by inspection of roentgenograms, according to simple rules based on the ratio of areas to volumes in the large series of human cholecystograms made by the senior author. While this method would not be sufficiently accurate to detect small differences, it has seemed adequate to reveal any gross differences in rate of emptying following excision of nerves.

2. Effect of eliminating specific nerves to the choledochoduodenal junction. As here outlined, the attempt was first made to eliminate *all* nerve fibers in the hepatoduodenal ligament converging upon the choledochoduodenal junction. But in 3 of the 11 cats in which the gall bladder reacted to food, although the gastroduodenal plexus was cut, the nerve was missed. In these 3 animals, therefore, the gastroduodenal nerve continued to function. Under these conditions the rate of emptying of the gall bladder seemed to compare favorably with the control data given by DuBois and Hunt (1932) for cats with intact nerves. As noted in Table II, A (cf. Fig. 2, row 1), the average time that elapsed before the gall bladders began to exhibit tonus was 6 minutes after food (controls, 9 minutes: Table I); the average time required for iodized oil to enter the cystic duct was 23 minutes (controls, 20 minutes); and the time required to empty the gall bladder was 275 minutes (controls, 269 minutes).

But when the gastroduodenal nerve was eliminated in addition to the fibers of the plexus, then a very different picture was presented—namely a marked retardation in rate of emptying (see averages for 8 animals in Table II, B and compare with Fig. 3, row 1). In fact the time required for emptying half or two-thirds of the contents of the gall bladder, was almost doubled from an average of 71 and 119, respectively (Table II, A) to an average of 165 and 232 minutes (Table II, B). While the number of animals in the first group is small, there is little overlapping of volumes, most of those for the second group being higher than comparable ones in the first group.

These observations, therefore, indicate that the gastroduodenal nerve carries fibers which lower the resistance at the biliary outlet. Further evidence that such fibers do not pass by way of the gastroduodenal plexus is that in animals 8, 9, and 12 of Table II, B, some fibers of the plexus escaped the ligatures, yet emptying of the gall bladder in these 3 was nevertheless retarded. The practical application to be made from these experiments is that severance of nerves to the choledochoduodenal junction in human patients should not be expected to lower the resistance to the flow of bile but rather to increase it.[1]

Turning now to the experiments on faradic stimulation of the cecum, it is clear that severance or ligation of the gastroduodenal nerve or plexus, or both, failed to affect or to abolish the inhibitory reflex from cecum to gall blad-

[1]The first attempt to relieve the pain of biliary dyskinesia in man by sectioning nerves in the hepatoduodenal ligament was performed by Reich (1940) in a patient that was being choledochostomized. Ten days after operation the intraductal pressure was found to be 85 millimeters of saline—40 millimeters less than the pressure obtained before operation. Injection of a quarter gram of morphine then caused a precipitate rise in pressure to 220 millimeters. Because this was not maintained for several hours, as in patients with an "intact sphincter," the author concluded that the 85 millimeter level represented a residual pressure due to the tone of the duodenum and that excision of the nerve, in this instance, had relieved spasm of the sphincter.

Until this single experiment has been verified, there are several *a priori* objections to it. First the average level of intraductal pressure in 24 choledochostomized patients was found by Bergh and Layne (1942) to be 120 millimeters of saline and to range from 110 to 240 millimeters. In another article of the same date Bergh showed that after egg-yolk the average fall in resistance was 70 millimeters, and that in one instance a spastic sphincter was lowered from 450 to 110 millimeters in 30 minutes. Therefore it would not seem that Reich's drop of 40 millimeters in 10 days is significant. Second, there is no evidence that severance of autonomic nerves affects the reaction of smooth muscle to morphine. Third, there is little known about the nervous pathways to the sphincter of Oddi in man, owing to the almost insuperable obstacle offered by the pancreas, so that in merely sectioning a nerve running horizontally behind the hepatic artery and approaching the bile duct just where it passes behind the duodenum there is no assurance that at this high level Reich may not have cut a nerve to the duodenum or pancreas.

TABLE II.—EFFECT OF CUTTING NERVES TO CHOLEDOCHODUODENAL JUNCTION

Cat	Time of feeding—hrs. after operation	Initial tonus in gall bladder min.	Oil enters cystic duct min.	Rate of evacuation of gall bladder—Minutes after food				Reflex—inhibition of gall bladder
				¼ empty min.	⅔ empty min.	¾ empty min.	Empty min.	
A. Gastroduodenal plexus cut or doubly ligated—Gastroduodenal nerve intact								
1	13	0	6	60	118	152	255	not tested
6	16	5	49	—	—	178	288	
7	15	7	15	82*	120	175 (⅞)	282	++
Average		2)12(6′	3)70(23′	2)142(71′	2)238(119′	3)505(168′	3)825(275′	
B. Gastroduodenal nerve and plexus cut or doubly ligated								
2	16	34	43	117(⅓)	380	—	—	+++
3	15	36	62	(none at 87′)	not tested	—	— 362	not tested
4	16	17	28	154	—	—	378(⅓)	
5	16	28	182+	336(⅓)	—	—	336(⅓)	++
8‡	14	16	73	140	227	—	428	+++
9‡	13	56	79†	—	—	—	411(1/10)	+++
12‡	16	5	47	120	149	—	291	++
14‡	16	19	47	125(⅓)	173	409	—	+++
Average		8)211(26′	8)568(71′	6)992(165′	4)929(232′		4)1492(373′	

*Fig. 2.
†Fig. 3.
‡A few fibers of the gastroduodenal plexus were missed. +Plus signs in last column indicate degree of relaxation.
Fractions in parentheses indicate nearest available reading, e.g., "(⅓)" after a figure in the "⅓ empty" column shows that only a third of the gall bladder had been evacuated.

der. In all of the 7 animals in which it was tried (see last column, Table II), the emptying of the gall bladder was stopped. The last 2 pictures in row 1, and the first in row 2, Figure 2, show how the column of oil in the cystic duct had dropped back within 45 seconds after the current had produced a spasm of the cecum, and how the gall bladder continued to relax after the second current was sent in. The middle 3 pictures of the second row show control experiments on the same animal and demonstrate that pinching the skin with forceps to produce the same amount of pain as spasm of the gut, did not diminish the tonus of the gall bladder, although a subsequent current lowered the tonus (last pictures in Fig. 2). These roentgenograms were taken of an animal (cat 7) in which the gastroduodenal plexus had been eliminated but not the nerve of that name. Those in Figure 3 are from a cat in which the gastroduodenal nerve was severed but not all the fibers of the gastroduodenal plexus (cat 9, cf. Table II, B). Here it can be seen (last 3 pictures of first row) that the current produced marked dilation of the gall bladder, whereas after pinching (first 3 pictures, second row) the phase of emptying, apparently just started, was not inhibited. Subsequently, induced spasm of the cecum caused marked fall in gall bladder tonus (last three pictures, second row).

These experiments would seem to prove, therefore, that stoppage of flow of bile from the gall bladder, as a result of visceral pain, is not dependent upon sphincter action and is not necessarily initiated by it, since the gall bladder can be inhibited in the absence of nerves to the choledochoduodenal junction. Conversely, Bergh (1942) has shown that in cholecystectomized patients, ingestion of egg-yolk will lower the initial resistance of the sphincter by an average of 7 centimeters of water. So it is apparent that both gall bladder and sphincter can work independently of

9:20 p.m., 7 minutes after food, yolk
9:37, 8 minutes later
9:53, 1 minute before current
9:54¾, 45 seconds after
9:56½, 2½ minutes after
9:57⅔, 50 seconds after second current
10:44, 82 minutes after food, 1 minute before pinching skin
10:45¾, 45 seconds after
10:47, 2 minutes after
10:49, 40 seconds after current

Fig. 2. Roentgenograms of the emptying of the gall bladder in cat 7 (as viewed from left side) after the *gastroduodenal plexus* had been interrupted. Note that the rate of emptying was not retarded (cf. No. 7, Table II, A) and that reflex inhibition of the gall bladder was not abolished, i.e. the column of iodized oil slumped (last two pictures, row 1) after faradic stimulation of the cecum (position of the latter indicated by 2-pronged electrode). Pinching of the skin (middle three pictures, row 2) did not cause loss of tone in gall bladder.

7:48 a.m.
9:10, 56 minutes after food, yolk
9:33, 79 minutes after food
9:46½, 1 minute before current
9:48¼, 45 seconds after
9:49, 1½ minutes after, 95 minutes after food
10:16½, 1½ minutes before pinching skin
10:18¾, 45 seconds after
10:19½, 1½ minutes after
10:36½, 1½ minutes before current
10:38¾, 45 seconds after
10:39½, 1½ minutes after, 145 minutes after food

Fig. 3. Roentgenograms of the emptying of the gall bladder in cat 9, after the *gastroduodenal nerve* had been interrupted. Note the initial delay in acquiring tonus, and the marked retardation in emptying (cf. No. 9, Table II, B). As in Figure 2, inhibitory reflexes caused by stimulation of the cecum were not abolished (last 3 pictures, rows 1 and 2) and pinching of the skin had no effect on emptying (first 3 pictures, row 2).

each other; i.e., there is no obligatory reciprocal mechanism.[1]

3. Effect of eliminating right or left vagus nerves. Since anatomically the dorsal (s. right) vagus seemed to contribute the only vagal component to the gastroduodenal nerve (inset, Fig. 1) and since severance of the latter retarded the flow of bile, it was next deemed advisable to study the effect of severing the right vagus nerve above the point where it divides into celiac and gastric divisions. The results of these experiments are shown in Table III, A and Figure 4.

In 6 animals the average time required for iodized oil to enter the cystic duct was 95 minutes (as against 20 for the controls and 71 for animals with a severed gastroduodenal nerve). To empty half the contents of the gall bladder, 219 minutes were required (as against 70 for the controls and 165 for the animals in which the gastroduodenal pathway had been cut). Analyzing the figures in another way, it appears that in 5 of these animals (last column, Table III, A), the gall bladders were in continuous contraction for an average period of 3 hours, yet in that time less than half the contents as expelled. But in the 12 controls, continuous contraction emptied two-thirds of the contents of the gall bladder in half that time (89.5 minutes, as computed from the figures and table of DuBois and Hunt).

From these observations it is apparent that when the right vagus is cut, there is not only an increased resistance to the flow of bile at the sphincter, but also decreased contractile force applied by the gall bladder, for the rate of emptying is much slower when the right vagus is cut than when merely the gastroduodenal nerve is eliminated.

This inference is substantiated by supplementary experiments in which the ventral (s. left) vagus was cut subdiaphragmatically—a nerve which sends no components to the gastroduodenal nerve (Fig. 1). In three such experiments (Table III, B) it was observed that it took an average of 152 minutes to empty half the contents of the gall bladder as against 219 minutes when the right vagus was cut, but that still the figure was much greater than the time required in the control animals (70 minutes, Table I).

The conclusions to be drawn from the above experiments are two: (1), that both vagi augment the power of contraction of the gall bladder; (2), that in addition, the right vagus, through its celiac division, sends inhibitory fibers to the sphincteric mechanism.[2]

4. Effect of eliminating the splanchnic pathways. When all the splanchnic roots to right and left celiac ganglia were cut (7 animals: Tables IV, A and A′, and Figure 5) the inhibitory reflex was abolished and the rate of emptying of the gall bladder was approximately that of the controls, i.e., half of the contents were emptied in an average of 86 as compared to 70 minutes, two-thirds emptied in 117 as compared to 104 minutes, and most of the contents in 238 as compared to 269 minutes (cf. Table I). The time required for initial tonus and for the oil to enter the cystic duct was somewhat greater, although pictures were not taken at sufficiently short intervals to secure accurate data. But when one considers the much greater shock to which these animals were subjected (for even under light anesthesia the animals jump when these nerves are cut) and the fact that the inhibiting reflex from cecum to gall bladder was abolished when the sympathetic pathway was interrupted (removal of which inhibition

[1] DuBois and Kistler (1933) in an ingenious study of the biliary tract in guinea pigs found that when the extraduodenal ampulla of the bile duct as well as certain poorly defined cords of the lesser omentum posterior to the common bile duct were stimulated faradically, contractions of the gall bladder could be recorded (by means of a heart lever attached to the fundus of the gall bladder). Also that severance of the common duct prevented the stimulation of the ampulla from causing contraction of the gall bladder, but that the latter responded to excitation of the hepatic end of the cut bile duct and of the vagi. From these experiments they concluded that in the guinea pig there is a direct nerve connection between the ampulla and the gall bladder. In the light of our work on the nerves of this region it is suggested that in stimulating the omentum, DuBois and Kistler may have been stimulating efferent branches of the left vagus (lesser curvature nerve) on their way to the gall bladder, and that in stimulating the hepatic end of the cut bile duct they may have been stimulating afferent fibers of the gastroduodenal plexus adjacent to the bile duct (cf. Fig. 1). Since the guinea pig has this highly specialized pumping apparatus, perhaps sensory nerves from the contractile ampulla play a rôle in regulating the activity of the gall bladder in this species.

[2] Although it has long been maintained that the vagi cause contraction of the gall bladder, it has only recently been verified by neurohistological methods (Sabussow and Ssuslikow, 1937). Forty-eight hours after section of the vagi in the dog, these authors removed the gall bladder, stained it with the Bielschowsky-Gros method and found a degeneration of the pericellular apparatus which embraces the ganglion cells lying external to the muscular tunic of the vesicle. From this they concluded that the vagus is motor to the gall bladder. They also observed that when both the vagi and the celiac ganglia were eliminated, the histological preparations of the gall bladder wall still retained some undegenerated postganglionic fibers. These were interpreted as being postganglionic to the intramural ganglia of the gall bladder, i.e., they belonged to the intrinsic nerve net. In this connection it should be recalled that when the biliary tract is stripped of all extrinsic nerves the gall bladder still empties in response to the hormones released by egg-yolk (Whitaker, 1926) although its rate of emptying, under such conditions, has never been determined.

8:33 a.m., 16 minutes after food
9:07, 50 minutes after food, yolk
9:18, 61 minutes after food
9:30¼, 74 minutes after food, 45 seconds before current
9:31¾, 45 seconds after
9:32¼, 90 seconds after
11:14, 177 minutes after food
12:43, 266 minutes after food
2:17, 360 minutes after food

Fig. 4. Roentgenograms of the emptying of the gall bladder in cat 35 after the dorsal (right) vagus had been severed. Note that the rate of emptying was greatly retarded (cf. No. 35, Table III, A). But, as in Figures 2 and 3, reflex inhibition of the gall bladder was not prevented by the operation (as demonstrated in last 2 pictures in row 1).

TABLE III.—EFFECT OF CUTTING VAGI AT ESOPHAGEAL HIATUS

Cat	Time of feeding—hrs. after operation	Initial tonus in gall bladder min.	Oil enters cystic duct min.	Rate of evacuation of gall bladder				Reflex inhibition of gall bladder	Period of sustained contraction* min.
				½ empty min.	⅗ empty min.	¾ empty min.	Empty min.		
A. Right vagus (and its celiac division)									
15	14	44−	122+	216 (¾)	—	401	—	++	
35	19	50−†	61−	177+†	—	—	360 (½)	++	205 (61–266)
37	20	48−	100‡	281	326	—	—	++	181 (100–281)
38	19	80§	196	324	—	—	—	++	128 (196–324)
39	19	29−	37−	192 (⅗)	—	—	347 (⅗)	++	185 (37–222)
40	18	25	55+	126 (2/5)	155	188	218 (5/6)	++	199 (55–254)
Average		6)276(49′	6)571(95′	6)1316(219′					5)898(180′
B. Left vagus									
41	18	22	78	192−	225	225	284 (¾)	++	114 (78–192)
46	15	15−	22	129−			338 (½)		
42	18	9	45	135	152	221	280 (¾)	++	90 (45–135)
Average		3)46(15′	3)145(48′	3)456(152′			3)902(301′		2)204(102′

*During which gall bladder discharged continuously, yet failed to empty more than half its contents.
†Fig. 4.
‡Emptying for 226 min. (100–326).
§Relaxes at 136 (emptying for at least 128′ (196–324)).

should increase the rate of emptying) it is probable that the slight reduction in the time required to nearly empty the gall bladder in this group of 7 animals should be interpreted as a slight acceleration of the rate of evacuation of the biliary tract.

This is confirmed by the second group of 7 animals (Table IV, B and B′). In these cats some of the fibers of the splanchnic pathway escaped section—either by way of the first and second lumbar roots of the celiac ganglia (B, Table IV) or in other types of experimentation (B′) when a few of the anterior branches of the celiac ganglia escaped. In such animals the inhibitory reflex from cecum to gall bladder was not abolished and emptying was retarded; i.e., when some of the fibers of the splanchnic pathway remained it took an average of 117 instead of 86 minutes to empty half the contents of the gall bladder, and 179 instead of 117 minutes to empty two-thirds of it. The difference is even more impressive if the comparison is restricted to the 5 animals in Table IV, B. There the corresponding figures would be 132 to 86, and 212 to 117. (In the 2 animals recorded under B′, in Table IV, only a few fibers escaped section, but these were enough to preserve the reflex.

The inferences to be drawn from these experiments are as follows. If section of the splanchnics may be considered to have somewhat accelerated emptying, the new rate must have been due to the fact that the operation abolished the inhibitory reflex from the cecum to the gall bladder.[1] The possibility remains, of course, that the splanchnics also maintained the tone of the sphincter and that when they were cut, the resistance was lowered and the rate of flow was thereby accelerated. However, since the acceleration was so slight and since section of the gastroduodenal nerve (through which the splanchnic fibers would pass) markedly retarded emptying, it is believed that some other agency than the sympathetic maintains the tone of the sphincter during fasting. It is suggested that this agency is local, perhaps the intrinsic nerve net

[1] Sabusson and Ssuslikow have given us a neurohistological picture of what happens in the gall bladder of the dog when both celiac ganglia are extirpated. When the wall is stained for nervous elements, degenerating bundles of myelinated nerves (afferent fibers ?) and degenerating terminal syncytia passing to the muscle fibers are found, but there is no degeneration of the pericellular apparatus around the ganglion cells. The authors interpret this to mean that postganglionic nerve fibers from the celiac plexus degenerate as far as the tissues in which they terminate.

7:52 a.m.
8:33, 33 minutes after food, yolk
8:43¾, 45 seconds before current
8:44¾, 45 seconds after
8:45½, 1½ minutes after
10:24, 144 minutes after food
7:51 a.m.
8:02, 7 minutes after food, yolk
8:29¼, 45 seconds before current
8:30¾, 45 seconds after
8:31½, 1½ minutes after
11:21, 206 minutes after food

Fig. 5. Roentgenograms of the emptying of the gall bladder in cats 28 and 27 after all splanchnic roots of both celiac ganglia had been severed. In cat 27 the lumbar sympathetic trunks were also severed. Note that the rate of emptying was not retarded by the operation (cf., respectively, with No. 28, Table IV, A; and No. 27, Table IV, A'), but that after sectioning the splanchnic nerves faradic stimulation of the cecum no longer inhibited contraction of gall bladder (see last two pictures but one, in each row).

TABLE IV.—EFFECT OF CUTTING SYMPATHETIC COMPONENTS

Cat	Time of feeding—hrs. after operation	Initial tonus in gall bladder—min. after food	Oil enters cystic duct min.	Rate of evacuation of gall bladder (min. after food)				Reflex inhibition of gall bladder	Pain
				½ empty min.	⅔ empty min.	¾ empty min.	Empty or nearly empty		
A. All splanchnic roots to celiac ganglia cut (symp. trunks intact)									
23	13	5−	5−	21	36	62	104	−	−
24	12	3+	45+	105	123	197−	252 (7/8)	−	−
28	15	22−	33−†	56+	90‡	120 (4/5)	200 (5/6)	−	−
34	12	38−	38	72	95‡	118	268 (7/8)	−	−
33*	13	34−	34	123	133	215 (5/6)	275	−	+
A′. All splanchnic roots to celiac ganglion cut, plus lumbar symp. trunks									
27	16	0	7†	52	120	155	206 (7/8)	−	−
26§	10	17	118	175	226	291	360 (5/6)	−	−
Average		7)119(17′	7)240(34′	7)604(86′	7)823(117′	7)1158(166′	7)665(238′		
B. Both major splanchnics cut (lesser and least splanchnics intact)									
18	19	7−	22−	83	162	215	293 (9/10)	++	
20	15	20−	58−	98	163		163 (3/3)	++++	
22	14	89−	108−	151 (3/8)	187	204+	204 (3/4)	++	
31	12	23	40−	142 (1/10)	300	300 (3/3)	300 (3/3)	+	
32	10	40−	64	185 (1/5)	250‡	−	308 (5/6)	+	
B′. Fibers of major splanchnics incompletely cut									
19‖	18	19−	35+	66	80‡	−	158+	++	
29¶	17	12−	47−	93	114‡	142	187 (9/10)	+	
Average		7)210(30′	7)374(54′	7)818(117′	7)1256(179′		7)1613(230′		

*Except root from L1 and L2 sympathetic ganglion (Fig. 6).
†Fig. 5.
‡Established by interpolation.
§Left lumbar sympathetic intact.
‖Left major splanchnic intact.
¶Anterior branches of celiac ganglia (leading to celiac artery) cut; some fibers escaped.

which surrounds the lower biliary passages (see figures by Schulze and Boyden, 1943). Indeed, it seems more reasonable to assume that in the long intervals of fasting the sphincter is kept closed by a local mechanism than by the intervention of extrinsic nerves.

Apparently, also, the sympathetic excitation of the gall bladder is much weaker than the vagal, since the retardation caused by severing the vagus is much greater than the acceleration obtained by severing the splanchnics. In this connection it should be recalled that inhibition of the human gall bladder cannot be induced by faradic stimulation of the stomach and duodenum, as in cats (Boyden and Rigler, 1934). Also it is possible that in man the vagus has lost its power to release the sphincter since its resistance is not lowered by neuromimetic drugs (Bergh, 2) and that this is accomplished only by antispasmodics and such hormone-producing substances as egg-yolk and magnesium sulfate (cf. Boyden, Bergh, and Layne, 1943).

5. Pathways of pain and of reflexes to the gall bladder from the cecum. Of special interest are certain incidental findings recorded in Table IV. First, in order to abolish reflexes from the cecum to the gall bladder it is necessary to cut both the major and the minor splanchnic nerves (i.e., to cut down to and include the rootlets of the first lumbar ganglion). Owing to variations it is probably

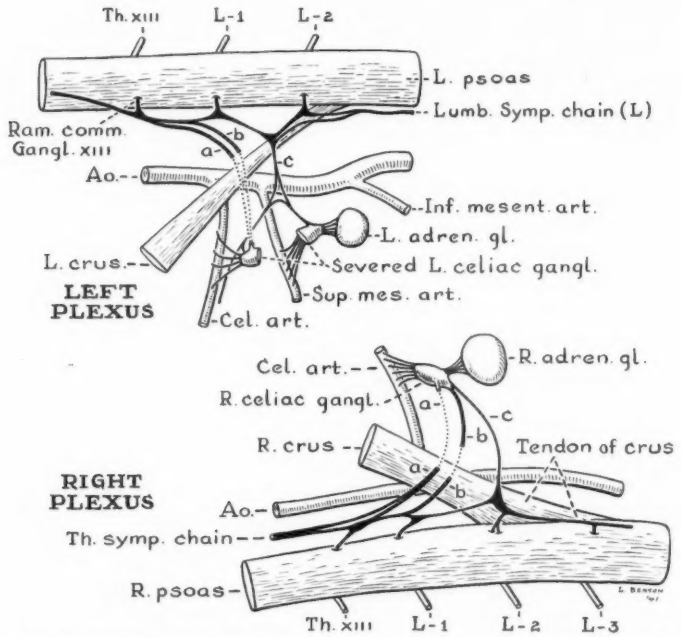


Fig. 6. Drawings made at autopsy of cat 33 (cf. Table IV, A). On both sides the greater, *a*, and lesser, *b*, splanchnics had been severed but not the least, *c*, splanchnic nerves. On the left side the celiac ganglion had also been bisected. Since, in this animal the inhibitory reflex to the gall bladder from the cecum had been abolished by section of nerves, it must have traversed the greater and lesser splanchnics. (The interrupted portion of this course is indicated by dotted lines). But pain following spastic contraction of the cecum, was not abolished, as when all splanchnics were severed (see other animals recorded in Table IV, A and A'); therefore pain impulses must have traversed the superior mesenteric plexus and least splanchnic nerves to have reached the lumbar segments of the spinal cord.

safer to cut the least splanchnics, also. But in order to abolish pain from the cecum it is necessary to cut all splanchnic roots as far down as the second lumbar sympathetic ganglion, i.e., not only the greater and lesser, but also the least splanchnic nerve. Evidence for this is shown in Figure 6 comprising drawings made at autopsy of Cat 33. In this figure the left plexus is drawn from the left side with the cat lying on its right flank; that of the right plexus, from the right side with the cat rolled over onto its left flank. On both sides the major, *a*, and minor, *b*, splanchnics have been cut, but the least, *c*, escaped. Under these conditions the inhibitory reflex was abolished but the pain still persisted. This suggests that the pain impulses reached the spinal cord through the superior mesenteric plexus, the least splanchnic nerve, and the ramus communicans of the second lumbar.

Second, these findings are contrary to the observations of Kuntz and Van Buskirk, who reported that complete decentralization of the celiac ganglia of the cat, following bilateral section of splanchnic and vagus nerves, does not abolish another type of inhibition of the biliary system, namely, secretion of bile during fasting. This inhibitory reflex is elicited by distention of the ileum and colon (Goldman and Ivy, 1939) or by faradic stimulation of the inferior mesenteric plexus. From such experiments Kuntz has inferred that reflexes may pass from the large bowel to the biliary tract without entering the spinal cord or traversing the splanchnic nerves; i.e., that such reflexes are mediated by the celiac ganglion. In view

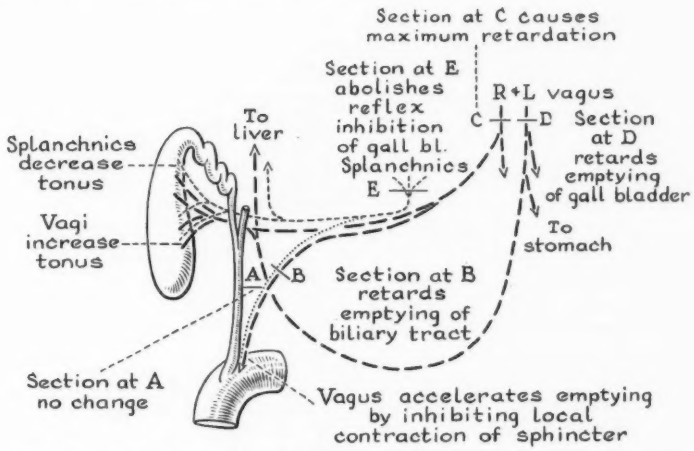


Fig. 7. Diagram summarizing the effects of sectioning various autonomic nerves (cf. summary in Table V). Area *A*, gastroduodenal plexus; *B*, gastroduodenal nerve.

of our difficulties in securing all the filaments, one wonders if the persistence of the reflex, as described by Kuntz, may not have been due to the failure of the operator to intercept all splanchnic nerves.

SUMMARY AND CONCLUSIONS

The effects of cutting or otherwise eliminating certain nervous pathways to the biliary tract in 34 cats are represented graphically in Figure 7 and assembled in Table V. They may be summarized as follows.

Severance of the gastroduodenal *plexus* to the choledochoduodenal junction does not affect the rate of emptying of the bile passages after ingestion of food nor abolish the inhibitory reflex to the gall bladder from the cecum. Presumably this plexus consists of afferent and vasomotor fibers.

Severance of the gastroduodenal *nerve* which innervates the same junction, markedly retards emptying. These observations raise serious doubt as to the efficacy of severing the nerves in the hepatoduodenal ligament of man as a means of treating a spastic sphincter, as recommended by Reich (1940).

Severance of the right vagus (and its celiac division) produces even greater retardation of

TABLE V.—SUMMARY OF RATE OF EVACUATION OF GALL BLADDER FOLLOWING SECTION OF NERVOUS PATHWAYS

Nervous pathway interrupted	No. animals	Initial tonus min.	Oil enters cystic duct min.	¼ contents gall-bladder discharge min.	⅔ discharge min.	All discharge min.	Reflex from cecum to gall bladder	
							Reflex	Pain
Lipoidol controls (DuBois and Hunt)	12	9^{9}	20^{10}	70	104	269	Not attempted	
Gastroduodenal plexus	3	6^{2}	23	71^{2}	119^{2}	275	+	+
Gastroduodenal nerve	8	26	71	165+**	234^{4}	373+†	+	+
R. vagus	6	49	95	219	—	—	+	+
L. vagus	3	15	48	152	—	301+‡	+	+
All splanchnic roots of celiac ganglion	7	17	34	86	117	238+§	o	o
Most splanchnic roots (some escaped section)	7	30	54	117	179	230+¶	+	+

Exponents indicate number of animals used in computing averages, when below full number.
*3 only ⅕ discharge. †2 only ⅓ to ½ discharge. ‡Only ½ to ¾ discharge. §2 only 5/6, 7/6. ¶3 only ¾–7/6.

flow, from which it is inferred that the right vagus not only sends parasympathetic inhibitory fibers to the sphincter region via the gastroduodenal nerve, but also motor fibers to the gall bladder via the hepatic plexus. The latter inference is substantiated by the fact that severance of the left vagus (which does not send fibers to the choledochoduodenal junction) also retards the emptying of the gall bladder, but to a lesser degree.

Severance of the splanchnic roots of the celiac ganglia as far down as the second lumbar nerve abolishes the inhibitory reflex from cecum to gall bladder, thereby somewhat accelerating the emptying of the gall bladder. Since cutting the nerve to the sphincter (gastroduodenal nerve) does not accelerate the flow but retards it, presumably this nerve does not convey sympathetic fibers charged with maintaining the tone of the sphincter. It is suggested, therefore, that during fasting the biliary outlet is kept closed through the action of a local mechanism, perhaps the intrinsic nerve net, and that after meals the tonic contraction of the sphincter is overcome by the right vagus and by hormones being formed in the intestinal mucosa. Since, in human patients the neuromimetic drugs have so little effect upon a spastic sphincter, it is possible that in man the vagus has lost its power to release the sphincter and that this is accomplished only by antispasmodics and hormone-producing substances.

These experiments also indicate that in the cat there is no obligatory reciprocal relationship between gall bladder and sphincter, since each responds to appropriate stimuli when the nerve to the other is cut. The vagus augments the tone of the gall bladder and inhibits contraction of the sphincter (thereby accelerating the flow of bile); the sympathetic exerts a temporary inhibiting effect on contraction of the gall bladder—a function that is apparently absent in man—thereby retarding the flow of bile from a viscus that is emptying under the influence of hormones and emanations from the vagus.

Pain impulses from faradically induced spasms of the cecum enter the spinal cord as low as the second lumbar ganglion, having traversed the superior mesenteric plexus and the least splanchnic nerves.

REFERENCES

1. Bergh, George S. Am. J. Digest. Dis., 1942, 9: 40-43.
2. Idem. Surgery, 1942, 11: 299–330.
3. Bergh, George S., and Layne, John A. Am. J. Digest. Dis., 1942, 9: 162–165.
4. Birch, Carroll L., and Boyden, Edward A. Am. J. Physiol., 1930, 92: 301–316.
5. Boyden, Edward A. Anat. Rec., 1928, 40: 147–192.
6. Boyden, Edward A., Bergh, George S., and Layne, John A. An analysis of the reaction of the human gall bladder and sphincter of Oddi to magnesium sulphate. Surgery, 1943 (In press).
7. Boyden, Edward A., and Grantham, Jr., Sam A. Surg. Gyn. Obst., 1936, 62: 34–42.
8. Boyden, Edward A., and Rigler, Leo G. Anat. Rec., 1934, 59: 427–447.
9. Carlson, A. J. J. Am. M. Ass., 1925, 85: 1468–1472.
10. Dubois, F. S., and Hunt, E. A. Anat. Rec., 1932, 54: 289–306.
11. Dubois, F. S., and Kistler, G. H. Proc. Soc. Exp. Biol., N.Y., 1933, 30: 1178–1180.
12. Kuntz, A., and Van Buskirk, C. Proc. Soc. Exp. Biol., N.Y., 1941, 46: 519–523.
13. Reich, Henry. Surg. Gyn. Obst., 1940, 71: 39–43.
14. Sabussow, G. H., and Ssuslikow, A. F. Zschr. Anat. Entw., 1937, 106: 739–748.
15. Schulze, John W., and Boyden, Edward A. The innervation and blood supply of the choledochoduodenal junction. Anat. Rec., 1943 (In press).
16. Wharton, L. R., Anat. Rec., 1937, 67: 469–475.
17. Whitaker, Lester R. Am. J. Physiol., 1926, 78: 411–436.

VAGINAL HYSTERECTOMY

W. C. DANFORTH, M.D., F.A.C.S., Evanston, Illinois

A GENERATION ago many hysterectomies were done vaginally. The gynecologists of the age of Joseph Price were skillful vaginal surgeons. As the safety of abdominal surgery increased, and as the attention of pelvic surgeons became fixed upon various phases of lower abdominal pathology, the vaginal route was used less frequently. Today, in some active clinics, the operation is carried out infrequently, the members of the attending staff hesitating to attempt it because of slight experience with it. This results in a deficient training of residents and internes in an important part of pelvic surgery. It also causes many women to be deprived of the method of surgical therapy which may be best adapted to the correction of the condition which they present. It is not wise to advocate that all hysterectomies be done vaginally, but it seems clear that the operation has a definite value and that at least some cases may be better managed by vaginal approach than by laparotomy.

Gynecological literature during the past few years has contained a number of papers which discuss the comparative merits of various methods of removing the diseased uterus. In many clinics the advantage of removing the cervix at the time the uterus is excised is stressed and the total abdominal operation is more frequently done, especially in well organized clinics, than it was some years ago. Total removal of the uterus may be accomplished either abdominally or vaginally, and the latter mode of attack lends itself very well to the treatment of many of the patients upon whom hysterectomy must be done. The advantages of the operation are not fully appreciated by some operators, and it is with the desire to discuss these that the present report is made.

In our service, for a number of years, we have done an increasing number of total operations in those cases in which the abdominal route was chosen. The increasing use of the total operation followed an experience of several years of work with the vaginal operation. As our number of vaginal excisions increased, we were struck by the fact that those patients whose cervices had been removed, as is the case when the uterus is taken out through the vagina, did not return to us for treatment of discharges from the cervical stump or because of bleeding from the same source. One of the greatest advantages of the vaginal removal is that the cervix is done away with. The danger of cancer in the retained stump is not a great one, although its existence must be acknowledged, but the stump may be troublesome as a source of leucorrhea, bleeding, and as a focus of infection.

In a series of 1510 hysterectomies of all types recently studied in our clinic the vaginal operation was carried out in 32.3 per cent. This series covers only the past few years during which time our technique has not varied. We do not believe that vaginal hysterectomy should be done in all cases, or in too great a proportion of the total number of patients operated upon, but we are convinced that the operation has a very definite value. In this report is considered a series of 517 vaginal hysterectomies.

In considering the indications for which these operations were done we find a number of conditions constantly named in the histories. Frequent among these are leiomyomas, prolapse, menorrhagia, retrodisplacement,outlet relaxation of greater or less degree, and endocervicitis or injuries of the cervix. In a very large part of these cases more than one of these conditions appear in the statement of indications. For example, leiomyoma with menorrhagia may be the major reason for deciding upon operation, but the patient may also have an unhealthy cervix and some cystocele or rectocele. It is difficult to classify the cases exactly according to indication as the combinations of conditions vary. Certain major reasons appear for the decision to adopt

surgical therapy. Among these we find leiomyomas of varying size, usually the smaller ones. Such tumors were the chief reason for operation in 170 cases. Prolapse is stated as the reason for operation in 144 cases. Many of these were extreme cases in which the uterus came well outside the introitus. Some, however, were less marked cases of descensus as the records indicate that the attending men in the service did not all have exactly the same idea as to the degree of descensus before the term prolapse should be used. Descensus of more moderate degree occasioned interference in 112 cases. Bleeding was the major indication in 53. In 50 cases in women past childbearing, a symptom-producing retrodisplacement was the reason for operation.

Nonmalignant bleeding, whether caused by small myomas or by dysfunction, is, in many cases, efficiently managed by vaginal hysterectomy. Both of these conditions are found for the most part in women who are nearing or who have reached the menopause and by far the greater number of them have had children. In many of them some outlet relaxation exists and a considerable number have cervices which are not healthy. All of these conditions may be remedied by one procedure which has the added advantage of preserving the ovaries. Irradiation for the relief of nonmalignant bleeding in women in the early forties frequently causes much discomfort because of the menopause which appears rapidly as a result of the destructive effect of the irradiation upon the ovaries. The preservation of the ovaries permits the menopause to come much more gradually, and the woman is far more comfortable than when the ovarian function is suddenly interrupted.

Larger myomas may be removed vaginally by excising the uterus piecemeal, or by morcellation. This is a procedure which demands a considerable degree of familiarity with the technique of the operation and which occupies a limited field. It should not be employed if an old subsided pelvic inflammation is present as the adhesions which this condition produces are extremely difficult to deal with from below. A simple form of morcellation, in cases in which the uterus is not very large but in which it is difficult to turn the corpus out anteriorly or posteriorly, is the amputation of the cervix. This converts the uterus from a relatively pear-shaped mass into an irregularly round one. The latter can be turned out much more easily and with the exhibition of far less force.

In the treatment of marked descensus and of prolapse, vaginal hysterectomy finds a place of real usefulness. In most of the clinics of this country prolapse is managed either by the excision of the uterus with interposition of the broad ligaments or by some form of the Manchester operation. The removal of the uterus has been our preference and our experience with this procedure has been a very satisfactory one. The objection that the uterus in many of these cases is normal is of little weight. In most of these patients it has no further function. In the majority, too, the cervix is not normal. It is lengthened, thickened, decubitus ulcers may be present, and the cervical canal is unhealthy. In the Manchester type of operation the cervix is usually removed. If the entire uterus is excised, not only the bases of the broad ligaments may be used for support but the upper portion as well may be utilized as a support for the bladder. In addition, if the uterus is removed the posterior herniation may be dealt with by uniting the uterosacral ligaments. This we have found to be one of the most important parts of the operation. The operation is nearly extraperitoneal and the patients, who in many cases are old women of deficient resistance, stand the operation very well. The tax upon the strength of the patient is far less than that which is caused by a plastic followed by an abdominal operation.

Women with symptom-producing retrodisplacement of the uterus, past the period of childbearing, are often more efficiently managed by the removal of the uterus than by any one of the various retrodisplacement operations. In patients at this time of life it seems more logical to remove the uterus than to do a more prolonged procedure which is intended to secure it where it belongs. In many of these women there are associated lesions of the vagina and cervix which may, with advantage to the patient, be cared for

at the same time. Subtotal hysterectomy has been recommended for this condition, but we have, in a considerable number of cases, chosen to deal with it by vaginal removal of the uterus, with vaginal plastic at the same time. In many of these cases the removal of a cervix which is often not normal is a further advantage. Removal of the uterus by any method is not advocated for this condition in young women.

Outlet relaxation together with a moderate descensus is a common finding in women in middle life. Both of these conditions may be cured at one time by the vaginal removal of the uterus. Small leiomyomas, endocervicitis, and menorrhagia are often present. Discomfort caused by sagging or retrocession of the uterus is often seen, and these conditions are frequently accompanied by outlet relaxation and more or less abnormality of the cervix. All of these may be corrected by one procedure with a minimal risk. The pelvic discomfort in many cases is the result of varicose veins of the broad ligament and these are done away with by the hysterectomy.

CONTRAINDICATIONS

Approach from below is contraindicated by a number of conditions. When hysterectomy is indicated in the presence of extensive residues of pelvic inflammatory disease the excision is best performed abdominally. The adhesions which may be found in these cases render the vaginal operation difficult and hazardous. Previous pelvic operations may be followed by adhesions sufficiently extensive to render vaginal work difficult. We have in a number of instances removed the uterus from below after some procedure for the shortening of the round ligaments had been done abdominally, but the operation has usually been difficult. It should not be attempted unless the operator has had a considerable experience with vaginal surgery. Patients upon whom suspension of the uterus to the abdominal wall for prolapse has been done are sometimes seen with the uterus again protruding. This procedure has disappeared from gynecological clinics. These patients may be operated upon from below, although it is sometimes difficult to bring the corpus of the uterus into the vagina until the false ligament which has often formed between the abdominal wall and the fundus uteri is severed. Access to this may be made much easier if an assistant presses down upon the lower abdominal wall. Cases in which endometriosis is suspected are better approached from above as the dense adhesions characteristic of this condition are hard to manage from below. Ovarian cysts, if not adherent, may be punctured and removed from below with no great difficulty, but the impossibility of being certain as to the exact character of the cyst before the abdomen is entered makes it wiser to treat them by abdominal incision.

We do not recommend the operation for the treatment of carcinoma of the uterine corpus. A very important early step in the performance of hysterectomy for corpus cancer is the blocking of the broad ligaments by placing straight 8 inch clamps alongside the uterus on either side to prevent the pushing out of cancer cells through the lymphatic vessels of the broad ligaments. This may be done immediately when the approach is made from above. When the operation is carried out from below the upper part of the broad ligaments is not occluded until late in the operation, while in the earlier stages the uterus will have been subjected to a considerable amount of handling. In most of the cases of corpus carcinoma, it is technically possible to remove the uterus from below, but the impossibility of early closure of the broad ligaments interposes a serious objection to the employment of the operation.

The technique of the operation used in our service has been described in a previous publication. The usual vaginal hysterectomy done in cases other than prolapse may involve only the removal of the uterus, but in most of these cases some form of vaginal plastic is also done. This may be only a perineal repair or an anterior plastic may also be necessary. If urinary incontinence exists, it may easily be cared for when the hysterectomy is done. The adnexa may be inspected through the vaginal wound.

We have continued to employ the operation with ligature of all divided tissues, and have not been impressed by the clamp method of

removing the uterus. This operation, in the days of poor suture material and deficient asepsis, no doubt played a useful rôle. Today the completer surgical methods seem more satisfactory.

In the series of 517 vaginal hysterectomies here reported, there has been no death. It must be conceded that there has been an element of good fortune in attaining so large a number without mortality. A well trained staff, proper selection of cases, and careful technique have played their part, but good luck has helped. It is scarcely likely that another similar number may be done without the loss of a single patient. Although mortality has been absent, morbidity has not. It is not possible to do hysterectomy by any method without some morbidity, as a bacteria laden area is invaded whatever the type of operation chosen. The morbidity is somewhat higher in the vaginal operation than in either the total or the subtotal abdominal hysterectomy. By the standard of the American College of Surgeons, that is, a temperature of 100.4 degrees on any 2 days excluding the first, 42.1 per cent of our cases must be placed in the morbid group. In spite of this fact, convalescence has been, as a rule, smooth. The hospital stay, in uncomplicated cases, is 11 or 12 days. Drainage is not used except in the cases of prolapse in which the dissection is rather wider than when the operation is done for other reasons. In cases in which the uterus protrudes from the introitus, and the broad ligaments are interposed between the bladder and anterior vaginal wall with the freed pubocervical fascia as an additional support, a small drain of rubber tissue is placed in the wound at the vaginal vault and is removed in 24 hours.

There were some more serious sequelae. Postoperative bleeding occurred in 15 cases. In all the cases in which bleeding occurred during recovery, it was easily controlled by a clamp or suture at the vaginal vault. In no case did a notable loss of blood occur. Pelvic abscess required opening in 7 cases. A vesical injury occurred in 3 cases. In 2 of these, after immediate repair, an uneventful convalescence followed. In 1 urinary extravasation caused some trouble, but the patient recovered. In 1 case a small nick in the rectum was made while doing a perineal plastic after the hysterectomy, but suture was followed by a smooth recovery. One old woman, after an operation for prolapse, had a cerebral hemorrhage on the 10th day, but recovered.

A common criticism of the operation is that it shortens the vagina. This, in our experience, has not occurred except in those cases in which the operation is done for extreme descensus. In these cases the anterior and posterior vaginal walls have been everted with the uterus and shortening has already taken place. In cases in which the uterus is at its normal level, or in which descensus is moderate, a vagina of normal depth may be left. When the uterus is totally excised, whether it is done abdominally or vaginally, if the vaginal wall is divided close to the cervix there will be no shortening or the difference in length will be so small that it will not be noticed. This has been true in so large a series of total hysterectomies by both methods that the fact appears to be definitely established.

Many of the technical difficulties of which some operators complain are due to the use of improper instruments. Bulky retractors and clamps not designed for use in this field take up so much of the limited space that work is impeded. Narrow curved retractors, fitting the bodily curves and occupying but little space in the field, are extremely useful. Proper clamps with rather shorter jaws than those used in the abdomen, and with a gentle curve, add to the ease with which hysterectomies other than those done for prolapse are carried out. It is wise to replace each clamp with a suture ligature immediately. This leaves the operative field free of dangling instruments which are in the way and is much more efficient from the standpoint of hemostasis. A small laparotomy pad, about 5 inches square, always with a tape attached, is useful after the uterus is out and while the remaining clamps are being replaced by sutures. Unmarked gauze should never be placed in the vaginal wound. Heavy catgut is unnecessary. No. 1 chromic gut is sufficiently heavy for the major ligatures and sutures and plain No. 1 or No. 0 for all others.

In many of our cases cystocele and urethrocele have been dealt with, and in a larger

number the perineum has been restored. When the patient is a nullipara, or if the perineum has been previously repaired, a small median episiotomy helps by giving greater exposure. This can be closed by sutures at the close of the operation.

While vaginal hysterectomy after previous pelvic surgery is, as a rule, inadvisable, we have, in a number of cases, removed the uterus from below after a laparotomy had been done. In nearly all these cases the previous operation had been for retrodisplacement or descensus. Vaginal hysterectomy after a retrodisplacement operation may be quite difficult, especially in the identification of the anterior peritoneal fold. In such cases the operator may solve the problem and keep out of danger by delivering the uterus posteriorly without having opened the anterior peritoneal fold, and, after having brought the corpus out, pass the finger up behind the uterus until the anterior fold is identified. It may then be opened without endangering the bladder. If the operation is done after a previous suspension for descensus a long false ligament between the fundus of the uterus and the anterior abdominal wall may cause some difficulty, although it may usually be reached and divided after the broad ligaments have been dealt with. In 1 case, because the true state of affairs inside the abdomen was not realized, the fundus was found firmly adherent over a considerable area to the anterior abdominal wall. The uterus could not be delivered. The fundal attachment was finally divided with difficulty, a thin layer of uterine tissue being left attached to the wall of the abdomen. This description merely indicates what may be done, but not what is advisable. When in doubt as to the state of affairs within the pelvis, it is best to make the attack from above.

One of our staff is studying the effect of the insufflation of a mixture of sulfanilamide and sulfathiazole into the vaginal wound as it is closed at the end of the operation. This mixture is blown into the space between the peritoneum and vaginal wall and upon the vaginal vault after closure. The result of this work will be reported later. The peritoneal invasion is limited in its area, and painstaking vaginal preparation before operation decreases the likelihood of introducing infection. The use of the sulfonamides may still further reduce this likelihood.

SUMMARY AND CONCLUSIONS

This series includes all cases done during a stated period by all the members of the department of gynecology and obstetrics of the Evanston Hospital, including the younger men of less experience. The operation properly carried out appears to be a very safe procedure and one which is followed, in most cases, by a rather smooth recovery. There is a definite morbidity which in nearly all cases is not severe. A few patients required attention to abscesses or bleeding. None of these presented a serious problem.

The operation has a definite value and should find a wider employment than it does. It has limitations which should be observed. Those who have had limited experience with it should select the easier cases for attack from below. With adequate experience many patients may be dealt with vaginally without difficulty. It is not wise to regard this procedure as one which may be used routinely or even in too great a proportion of all cases. With proper selection of cases and with an adequate technique it is an extremely useful addition to operative resources. The pelvic surgeon should be sufficiently master of the various methods of removing the uterus that his choice of procedure may be based wholly upon the conditions presented in each case. It should not be influenced by lack of familiarity with any one of the available methods.

EXPERIMENTAL PRODUCTION OF BRONCHIAL FISTULA IN RATS AND RABBITS

ALVIN CARLSON, M.D., and W. E. ADAMS, M.D., F.A.C.S., Chicago, Illinois

THE purpose of this research was to provide a means by which carcinogenic substances could be applied directly to the bronchial mucosa of rabbits and rats in an attempt to produce bronchogenic carcinoma. Many methods have been used in the past to produce lung tumors in susceptible animals. Carcinogens have been rubbed on the skin (3) and have been injected intravenously (5), subcutaneously (2), and intratracheally (6). They have been applied on threads which have been threaded through the chest cavity (2). Susceptible animals have been subjected to atmosphere laden with dusts (4). The results of these methods were largely the production of lung tumors which seemed to arise from alveoli and were predominantly subpleural in distribution. They contained few mitoses and showed slight or no tendency to metastases. More important, they had no relations to the bronchioles and were not true bronchogenic tumors.

It was our thought that if we could produce a permanent bronchial fistula in animals which were susceptible to induced tumors, we could possibly produce a more typical lung tumor by repeated application of carcinogenic substances directly to the bronchial mucosa. Adams and Livingstone in 1931 described a method for the production of bronchial fistulas in dogs. With several modifications this principle was found applicable to rats and rabbits.

METHOD IN RATS

Adult white rats were used in these experiments and ether anesthesia was administered through a loosely fitting face mask. The left chest was used routinely because only one large lung lobe is present on this side in rats. This made the procedure easier, more uniform, and above all the resulting fistulas were larger and easier to keep open.

At the beginning, a two stage procedure was used. The chest wall was opened through the left 5th interspace and the lung lobe brought out through the incision. Pericostal sutures were then placed on either side of the lobe and the ribs brought together fairly tightly about the exteriorized lung. The muscles and skin were then brought together over the lobe thus completing the first stage. The second stage was performed 5 to 10 days later in order to give time for healing and fibrosis to take place between the lung tissue and the chest wall. The wound was then reopened and the lobe cut off a short distance from the chest wall. The bronchus was identified by probing and a foreign body inserted to keep it open. The skin was sutured to the underlying muscles and the wound was left wide open.

The method mentioned of producing bronchial fistulas was found to be unsatisfactory, yielding only 25 to 50 per cent desired results for the following reasons: There was no way to determine accurately the tension on the pericostal sutures and they were frequently either too tight or too loose. When they were too tight the lung tissue would completely slough before the second stage; and when they were too loose, the lobe would either slip back into the chest cavity or marked bleeding would take place when the lobe was cut off. This bleeding was very troublesome because even if we did manage to stop it before the animal died, we would frequently have the main bronchus also tied off because of its very close proximity to the main vessels.

These problems were solved by performing the whole operation in one stage. The lung lobe was brought out through the 5th interspace and the pericostal sutures were placed as mentioned. Then the lobe was immediately cut off a short distance from the chest wall. No bleeding occurred if the stitches

From the Department of Surgery, The University of Chicago.
This work has been conducted under a grant from the Douglas Smith Foundation for Medical Research of The University of Chicago.

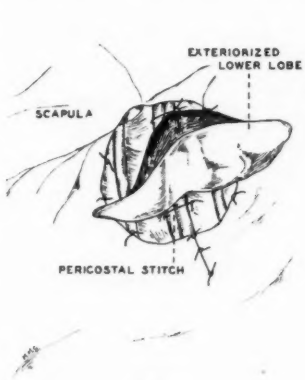


Fig. 1.

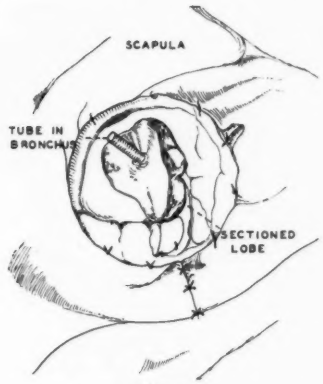


Fig. 2.

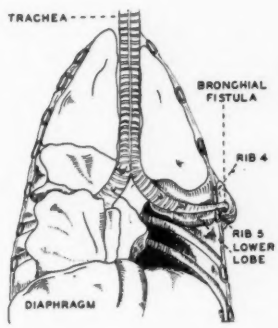


Fig. 3.

Fig. 1. The lung lobe is exteriorized and the adjacent ribs are brought together about the hilus.

Fig. 2. The exteriorized lung lobe has been cut off and a foreign body has been inserted into the bronchus.

Fig. 3. A ventral section through the chest of a rabbit to show the relations of the trachea, bronchus, and fistula.

were reasonably tight. The bronchus was then identified and a short piece of twine was inserted. The wound was then closed about the twine and one suture was taken through the twine and the skin as a means for keeping it immobile. About 5 days later when the twine could be removed, a fistulous tract was left which was wide open and quite straight.

Eighteen rats were operated upon by the method described. Three died at operation apparently from too much ether. Two died of tracheal obstruction caused by the twine slipping inward. Three did not develop fistulas because the twine slipped out. Ten rats developed large fistulas demonstrable by x-ray with iodized oil injection.

Before we were able to obtain uniformly good results two major problems presented themselves. The first was to get the animals to survive the open pneumothorax. In rat operations, speed and dexterity proved to be the answer. Immediately after the pleural cavity was opened the pericostal sutures were placed. The chest wall was kept closed at all times by the assistant, except while the lung lobe was being brought out. After first few operations it was rare to have a rat die on the operating board from open pneumothorax.

The second problem involved the material to be used to keep the bronchus open. Rubber and metal tubes and cotton and gauze packing were tried but none would stay in place long enough to give the superficial tissues time to heal. We finally tried ordinary wrapping twine (about 10 turns to inch) which solved the problem. Because this twine swells when it absorbs moisture, it stayed in place and kept the bronchus dilated while the wound healed.

METHOD IN RABBITS

The principle of the production of bronchial fistulas in rabbits was the same as that in the rats and only differences in technique will be elaborated.

Rabbits have much less resistance to infection than do rats; therefore it was necessary to perform operations with more attention to sterile technique. In spite of this precaution, many rabbits died with a profuse pleural infection, developed either at or after operation.

Because rabbit lungs were found to be more friable and more difficult to bring out of the chest cavity, some method other than speed had to be developed to combat the pneumothorax. A positive pressure ether apparatus was devised which proved adequate. The positive pressure was not applied until the rabbit was deeply anesthetized because otherwise laryngeal spasm forced the ether mixture into the stomach. With this apparatus we were able to keep rabbits alive with open chests for as long as 1 hour.

Specially made brass plugs were found to be the best means for keeping bronchi open.

Fig. 4. X-ray film with iodized oil showing bronchial fistula in a rat.

They were pointed and grooved at one end to facilitate introduction into the bronchus.

It was also found advisable to immobilize the rabbits' forelegs during the first 6 to 8 postoperative days because their scapulas and elbows were constantly disturbing the operative field. For this purpose, gauze soaked in starch was used to good advantage.

Operations were performed on 24 rabbits by the technique described. Eight died at operation either from too much ether or from a lack of air exchange. Six died after operation from profuse chest infections. Ten developed open bronchial fistulas demonstrated by x-ray with iodized oil injection.

Both rats and rabbits with bronchial fistulas require constant attention in order to keep the fistulas open. If they are left alone without twine or tube in place, the fistulas heal spontaneously within a very short time.

While these experiments were going on, and also at the present time, these fistulas were being treated with carcinogenic substances, notably, benzpyrine. Applications were made every other day for as long as 3 months with no definite gross evidence of cancer being found.

In addition, studies are being carried out on the effect of exteriorization *per se* on lung tissue. These are not complete enough to report at the present time, but indications are that some metaplasia of bronchial mucosa takes place in addition to the production of fibrosis and atelectasis.

Fig. 5. X-ray film similar to that in Figure 4, showing bronchial fistula in rabbit.

SUMMARY

1. Production of persistent bronchial fistulas in rats and rabbits is deemed worth while because of the possibility of inducing true bronchogenic tumors by direct application of carcinogens to the bronchial mucosa.

2. Procedures are described for the experimental production of persistent bronchial fistulas in rabbits and rats.

3. Results of treatment of bronchial mucosa directly through the fistula with the carcinogen benzpyrine for a period of 3 months are grossly negative.

4. The possibility that lung tissue is changed morphologically by exteriorization *per se* is mentioned and is being studied further.

REFERENCES

1. Adams, W. E., and Livingstone, H. M. Surg. Gyn. Obst., 1931, 53: 479.
2. Andervont, H. B. Pub. Health Rep., Wash., 1937, 52: 1584.
3. Samssonon, M. Am. J. Cancer, 1940, 39: 255.
4. Seelig, M. G., and Benignus, E. L. Am. J. Cancer, 1936, 28: 96.
5. Shimkin, M. B. Arch. Path., 1940, 29: 229–253.
6. Idem. Am. J. Cancer, 1939, 35: 538–542.

BENIGN TUMORS OF THE LARGE INTESTINE—

Incidence and Distribution

ELSON B. HELWIG, M.D., St. Louis, Missouri

A COMPARISON of the published reports dealing with the incidence and occurrence of benign tumors of the large intestine shows a marked discrepancy in the prevalence of these tumors. This discrepancy may be accounted for in a number of different ways. Thus, if the specimens for study have been removed at surgical operation only those tumors which have produced symptoms are likely to be included. If the material for study is obtained from autopsies the incidence will vary with the care taken to note the presence of the tumors. And, finally, when the incidence of tumors is determined upon the basis of a small series of cases, the results are less likely to be reliable.

The term polyp is commonly used to designate any benign tumor either sessile or pedunculated arising from the mucous membrane of the large intestine. While this interpretation of the term polyp may convey the gross conception of the tumor, it does not signify the essential pathological structure of the tumor. On the basis of the exact structure, this group of tumors referred to grossly as polyps may be classified into a number of different types such as adenomas, leiomyomas, carcinoids, and lipomas. Since each type of tumor is characterized by a distinct clinical course and prognosis the necessity of an accurate diagnosis is obvious. The explicit nature of the polyp must be known in order to arrive at the correct treatment and prognosis. In this study of the large intestine, the occurrence and exact nature of each polyp was determined.

MATERIALS AND METHODS

This report is based upon 1,460 consecutive autopsies in which the entire large intestine was available for study. Each intestine was carefully examined in the fresh state. All grossly discernible elevations and irregularities of the mucosa were recorded and the distance of each was measured from an anatomical landmark. Each elevation, together with the adjacent intestinal wall, was removed and placed in 10 per cent formalin. After fixation, sketches of each lesion and the pertinent descriptive information were recorded on an anatomical drawing of the large intestine. Large lesions were sectioned in a plane perpendicular to the mucosa. All blocks of tissue were then embedded in paraffin in such a manner that the plane of section was at a right angle to the plane of the mucosa. Single sections and in many instances step and serial sections were prepared and stained with hematoxylin and eosin. The microscopic appearance of the lesion was then noted and studied in relation to the gross appearance. On the basis of the microscopic structure, the exact diagnosis of the lesion was established. All carcinomas and sarcomas have been excluded from this study, although a small number of adenomas showing microscopic foci of carcinoma have been included. The adenomas containing foci of carcinoma will be discussed in detail in another communication. Also all lesions obviously the result of inflammation, thrombosed hemorrhoids, and anal fibrous tags have been excluded.

From the Department of Pathology, Washington University School of Medicine, St. Louis.

TYPES OF POLYPS

The number of cases and the various types of polyps encountered in the large intestine in this series are as follows:

Adenoma, 139; lipoma, 13; carcinoid, 1; leiomyoma, 1, a total of 154 cases.

Adenomas. In the 1,460 consecutive large intestines studied there were 139 which contained adenomas, an incidence of 9.5 per cent. Omitting one instance of familial polyposis, the remaining 138 contained a total of 272 adenomas. In 80 instances there were single adenomas and in 59 cases 2 or more adenomas

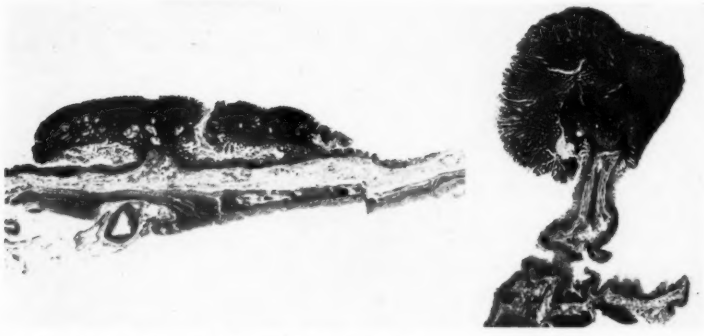


Fig. 1, left. Adenoma of the sessile type. ×3.6.
Fig. 2. Adenoma of the pedunculated type. The stalk is covered with normal mucosa. ×2.

were present. Table I shows the incidence of adenomas in the colon and rectum.

TABLE I.—INCIDENCE OF ADENOMAS IN COLON AND RECTUM

	Adenomas solely in one site		Adenomas present in both sites		Total	
	Cases	Per cent	Cases	Per cent	Cases	Per cent
Colon...	103	7.05	17	1.15	120	8.22
Rectum.	18	1.26	17	1.15	35	2.39

In this series the incidence of adenomas in the colon, 8.22 per cent, was appreciably greater than that reported by others. Stewart found 4.19 per cent in 1815 autopsies; Susman, 6 per cent in 1100 autopsies; and Lawrence, only 2.37 per cent in 7,000 autopsies. Lawrence attributed the low incidence in his series to the large number of children included, 25 per cent of the 7,000 autopsies being on children under 11 years of age. However, in the present study the percentage of autopsies of children less than 11 years of age was also 25 per cent. In the 1,460 autopsies the incidence of adenomas in the rectum was 2.39 per cent compared with the observation made by Lawrence of 0.42 per cent. In both series approximately one-half of the intestines with adenomas in the rectum also showed adenomas in the colon. In the present series the number of adenomas noted in the rectum was about five times the number recorded by Lawrence, and the number of adenomas of the colon was three times the figure reported by the same author. However, in general, the relative incidence of adenomas in the rectum and colon was in agreement with the observation of Lawrence and in disagreement with the experience of Swinton and Warren. The identification of the adenomas studied by Swinton and Warren was dependent largely on roentgenographic and proctoscopic examinations. These workers were able to visualize 70 per cent of the tumors in their series through a 10 inch sigmoidoscope. Obviously the greatest number of adenomas would be encountered in that segment of the large intestine in which the sigmoidoscope is applicable. It would appear doubtful that this highly selected material could give the true incidence of adenomas of the rectum and colon.

Table II shows the distribution of the adenomas.

TABLE II.—DISTRIBUTION OF ADENOMAS

	Cases	Per cent
Cecum	32	11.8
Ascending colon	42	15.4
Hepatic flexure	12	4.4
Transverse colon	32	11.8
Splenic flexure	13	4.8
Descending colon	22	8.1
Sigmoid colon	76	27.9
Rectum	43	15.8
Total	272	

From Table II it is seen that the sigmoid colon is the most common site in the large intestine for the occurrence of adenomas, 27.9 per cent occurring in this segment. Saint found 20 of 51 polyps located in the sigmoid

Fig. 3.

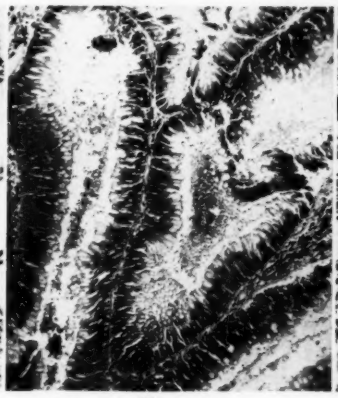


Fig. 4.

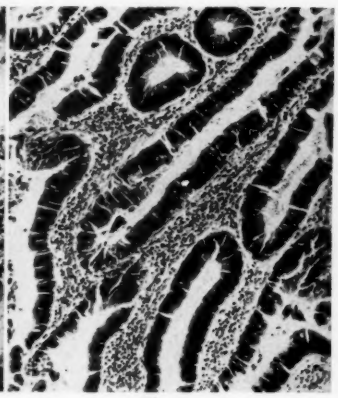


Fig. 5.

Fig. 3. Photomicrograph of the adenoma shown in Figure 1. Note variation in type of cells lining glands. ×85.

Fig. 4. Photomicrograph of a section through the periphery of the adenoma which is shown in Figure 2. The cells are tall, columnar and contain mucus. ×85.

Fig. 5. Photomicrograph of the base of the adenoma shown in Figure 2. The cells lining the glands are columnar but do not contain mucus. ×85.

colon, although it is not clear that all of the tumors were adenomas. In an analysis of 166 cases of adenomas of the colon, Lawrence found the sigmoid colon involved 43 times. In an additional 13 cases the sigmoid colon was involved as part of a generalized polyposis of the colon. The observations in the present study are in agreement with the experiences of Saint and of Lawrence, that the sigmoid colon is the most commonly involved site.

The adenomas may be either sessile (Fig. 1) or pedunculated (Fig. 2). A few were as small as 1 millimeter in diameter and the largest measured 9 centimeters in the greatest diameter. Numerous adenomas studied in the one case of multiple polyposis involving the entire colon and rectum in this series were similar in all characteristics to the solitary and multiple adenomas in the other cases.

Histological studies of the adenomas revealed a variable structural and cytological picture. The supporting framework ranged from a single, simple connective tissue stalk to multiple complex branching cores of connective tissue. In some instances the muscularis mucosae extended upward from the wall of the intestine into the pedicle, and in others only isolated foci of smooth muscle were noted in the stalk. The stalks contained a variable but usually moderate number of small and large blood vessels. The normal mucosa of the intestine either terminated at the base of the adenoma or, particularly if the polyp was of the pedunculated type, covered the base and stalk. Regularly arranged columnar epithelium disposed in the form of glands covered the connective tissue stalks. The glands varied in size and contour. The columnar epithelium ranged from cells with pale acidophilic cytoplasm to cells of the goblet type with clear cytoplasm. In some instances an entire adenoma showed a single type of cell and in other examples a single polyp exhibited variations of cell type (Fig. 3, 4, 5). Thus one adenoma would be comprised entirely of mucus-filled cells whereas another would exhibit only a few, if any, cells of this type. Mitotic figures were encountered frequently in some adenomas and were uncommon in others. From the aforementioned description it is apparent that not only was there variation among different adenomas but that a single or solitary adenoma frequently exhibited a pronounced variation in structure.

Lipomas. The lipomas constitute the second most frequent group of polyps found in the large intestine. In the 1,460 consecutive large intestines observed in the present series, 13 contained lipomas, an incidence of 0.89 per cent. Comfort found 20 submucous intestinal lipomas in 3,924 consecutive autop-

Fig. 6. Lipoma of the pedunculated type. ×2.5.

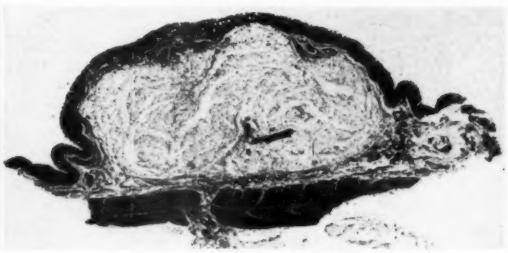


Fig. 7. Lipoma of the sessile type. ×4.6.

sies. Ten of these were located in the large intestine, an incidence of 0.25 per cent. Staemmler noted only 9 cases of lipomas of the entire intestinal tract in 17,000 autopsies, an incidence of 0.05 per cent. The greater incidence recorded in the present series is probably the result of a more careful examination.

In the present group of 13 large intestines, 10 showed a solitary lipoma and 3 contained 2 or more. Of the 3 instances of multiple lipomas, the cecum and ascending colon were involved in 1 instance, the ascending colon and sigmoid in another, and only the cecum in the third. The distribution of the lipomas was as follows:

Of a total of 20 cases the lipomas were in the cecum in 9 cases; in the ascending colon in 8 cases; in the descending colon, sigmoid colon, and rectum in 1 case each; while none was found in the hepatic flexure, transverse colon, or splenic flexure.

The cecum and the contiguous ascending colon are the most common sites of lipomas in the large intestine. This result is in agreement with the conclusion of Comfort and contrary to the observations of Stetten. Stetten, analyzing cases from the literature, found the predominant site of lipomas to be the sigmoid colon and rectum. Both the sigmoid colon and rectum were involved more frequently than either the cecum or ascending colon. In the analysis made by Stetten the presence of some of the tumors was noted because of clinical symptoms. Since the rectum and sigmoid colon are accessible for direct examination, the identification of the tumors in these locations was probably more readily established.

The distribution according to sex showed 4 men and 9 women, although the ratio of male to female autopsies was about 3 to 2. Comfort, analyzing the reported lipomas of the entire gastrointestinal tract, noted the cases about equally divided between the two sexes.

TABLE III.—OCCURRENCE OF LIPOMAS

Age group	Intestines Examined	Cases of Lipomas
Under 50 years	838	1
50 to 60	255	4
60 to 70	206	6
70 to 90	161	2

Table III shows the age of the patients in whom the lipomas were encountered. With the exception of one patient, a man 31 years of age, all were over 50 years of age. Thus the incidence of lipomas is greatest in the same decades in which adenomas and carcinomas are most common.

The lipomas of the intestine may occur in either the submucosa or the subserosa and more rarely involve both sites. In the present study of 13 cases the submucosa was the site involved in 12. In the other case the tumor was located in the subserosa of the sigmoid colon but produced an elevation of the mucosal surface. Incidentally, this was the only lipoma of the large intestine found in a patient under 50 years of age.

Two of the large intestines containing lipomas also contained adenomas. Furthermore, 2 other large intestines with lipomas presented a carcinoma. Thus in 4 of the 13 cases of lipoma there was another type of tumor involving the large intestine. This fact may signify a special susceptibility in these patients to the development of tumors.

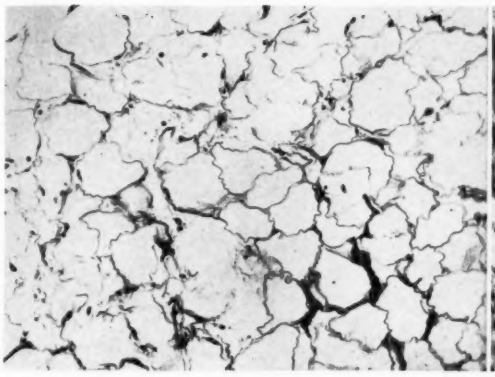


Fig. 8. High power photomicrograph of the lipoma shown in Figure 7. The fat cells are of the adult type. ×100.

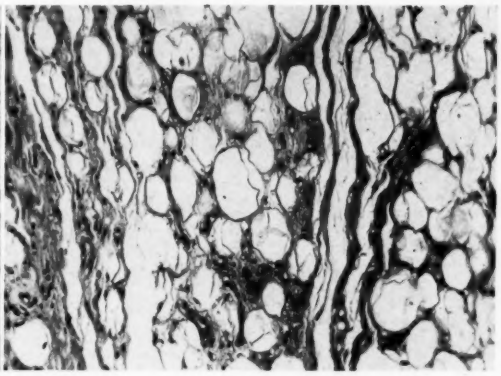


Fig. 9. High power photomicrograph of the lipoma shown in Figure 6. Some of the cells are cuboidal and fusiform with a granular and vesicular cytoplasm. ×100.

In 3 of the 12 cases of submucosal lipomas there were single pedunculated tumors (Fig. 6). The lipomas of the 9 other cases were sessile (Fig. 7). Grossly the tumors were soft, smooth, and pale gray or grayish-yellow. The pedunculated lipomas were attached to the wall by narrow flat stalks. These tumors were oval in shape and flattened in one dimension.

Histologically the tumors were comprised of the adult type of fat cell (Fig. 8). The fat cells were arranged in groups of variable size which were separated by irregular connective tissue trabeculae. The trabeculae were usually delicate, but in a few instances the connective tissue was relatively abundant. Blood vessels, usually small, were dispersed throughout the septa. Peripherally, the lipomas were surrounded by a thin but variable zone of connective tissue. Occasionally this layer of connective tissue was poorly defined. Although Staemmler described an immature type of fat cell at the periphery, none was noted in this location in this series. However, within some of the lipomas cuboidal or fusiform cells with a granular and vesicular cytoplasm were noted (Fig. 9). Except for scanty collections of lymphocytes there was no infiltration of inflammatory cells, although a few lymphoid nodules were sometimes present at the level of the muscularis mucosae. Thus these lipomas

Fig. 10. Leiomyoma of the pedunculated type. The tumor is separated from the muscularis by a stalk of connective tissue. ×3.6.

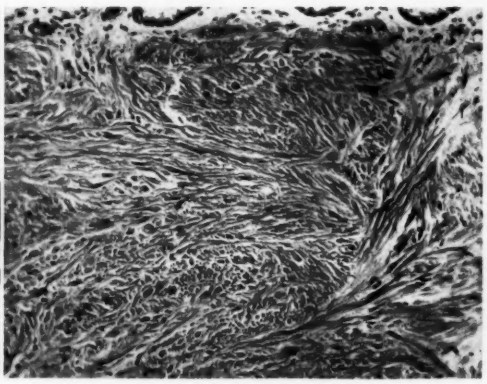


Fig. 11. Section of leiomyoma shown in Figure 10. The tumor is composed of interlacing bands of smooth muscle cells, and is continuous with muscularis mucosae. ×110.

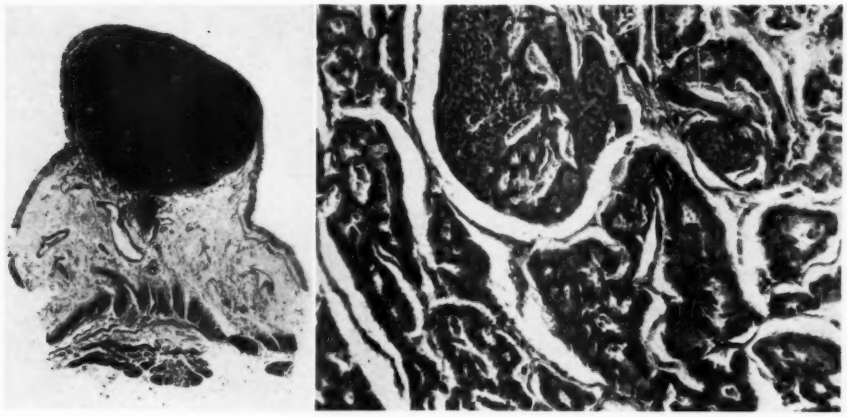


Fig. 12, left. Carcinoid of the rectum. Note the intact layer of mucosa. ×2.8.
Fig. 13. Photomicrograph of the carcinoid shown in Figure 12. The cells are arranged in cords and in alveolar structures. ×110.

have not produced evidence for the origin of the tumors on an inflammatory basis. In the smaller tumors there was no disturbance of the muscularis. In the larger lipomas, the muscularis was slightly compressed and distorted by the tumor. The muscularis mucosae varied from a well defined layer to only thin remnants. The tumors in all instances were covered on the lumen surface by mucosa. The most outstanding change of the mucosa was an attenuation of the glands and decrease in the width of this layer. The goblet cells in some instances were prominent but for the most part were not noticeably changed. In a few instances the capillaries of the mucosa were distinctly dilated and hyperemic.

The clinical diagnosis of a lipoma of the intestine frequently rests upon the presence of a complication such as obstruction, intussusception, or spontaneous expulsion. If only those cases which have produced obvious clinical signs are recorded, the incidence of lipomas of the colon would appear abnormally low. This study based on autopsy material indicates that the actual incidence is much greater. Many lipomas of the large intestine probably never produce manifest clinical symptoms.

Leiomyoma. Only one tumor composed of smooth muscle was encountered in this series of 1,460 autopsies. It was located in the sigmoid colon of a 67 year old man and formed a pedunculated firm mass measuring 11 millimeters in the greatest diameter (Fig. 10). The mucosal surface was smooth and reddish-brown. Histologically the tumor was comprised of elongated smooth muscle cells with a tendency to be arranged in interlacing bands (Fig. 11). A few small blood vessels were present within the tumor. No mitotic figures or giant cells were noted. The tumor was poorly delineated from the muscularis mucosae and was not encapsulated. Golden and Stout have pointed out that the lack of a capsule of the intestinal leiomyoma may be used in differentiating this tumor from nerve sheath tumors. The stalk consisted of connective tissue within which were several small and large blood vessels. There was no connection between the muscularis and the tumor. The pedicle and most of the tumor were covered by an essentially normal mucosa. One segment of the mucosa surmounting the tumor showed fibrosis of the stroma. This area might possibly represent a former site of inflammation. The indefinite demarcation of the tumor from the muscularis mucosae suggested that the latter was the point of origin.

Leiomyomas of the large intestine are uncommon. Golden and Stout did not encounter a single leiomyoma of the large intestine in

5,869 autopsies although 8 cases were garnered from specimens obtained from surgical operation. However, such material does not form a reliable index of the true incidence of disease processes. Comfort, probably referring to the entire gastrointestinal tract, stated that lipomas occur in approximately the same frequency as myomas. In the present study of large intestines the lipomas were much more common than the leiomyomas.

Golden and Stout have recently made a comprehensive analysis of leiomyomas of the gastrointestinal tract which have been reported in the literature. In addition to the submucosal location of the tumor as described in this report the tumors may be subserosal, intramural or combined subserosal and submucosal.

Carcinoid. The fourth type of polyp encountered in this series was the carcinoid or argentaffinoma. The carcinoid occurs most commonly in the appendix and less frequently in the ileum. As determined by the reports in the literature it is a decidedly uncommon tumor of the large intestine. Ashworth and Wallace, in a review of unusual locations of carcinoid tumors, found 11 cases in addition to 1 of their own in which the tumor was located in either the colon or rectum. Two tumors were located in the cecum, 2 in the sigmoid colon and 2 in unspecified sites. The 5 remaining tumors were situated in the rectum.

In the present report the tumor was located in the rectum of a man 56 years old. Grossly the tumor formed a firm hemispherical elevation measuring 15 millimeters in the greatest diameter, which projected into the lumen of the intestine (Fig. 12). A smooth but otherwise normal-appearing mucosa covered the nodule. The entire nodule moved freely with the submucosa, but the mucosa was closely affixed to the tumor. The cut surface of the tumor was grayish yellow.

Histologically the layer of mucosa was thin but intact. The muscularis mucosae formed a generally distinct but thin layer beneath the mucosa. There were lymphoid nodules centered at this level. Bounded by the muscularis mucosae and occupying the submucosa was a nonencapsulated nodule of tumor (Fig. 13). The cells of the tumor were arranged in nests and more frequently in cords, which often exhibited a disposition to intercommunicate and form alveolar structures and pseudorosettes. The cells were either polygonal or cylindrical and the cytoplasm, pale and acidophilic. The nuclei were either round or oval and contained a moderate number of fairly evenly distributed chromatin granules. No mitotic figures were noted. When the cells were cylindrical and arranged in columns, the polarity of the nuclei within the cells varied but the shape and size of the nuclei were remarkably uniform. The nests and columns of cells were separated by a stroma of connective tissue which ranged from fine septa to large dense bands. Small blood vessels were present within the stroma. A few collections of tumor cells were noted within the muscularis mucosae. The base of the nodule showed nests of tumor cells extending irregularly into the submucosa. However, this layer was greatly thickened so that a wide zone of connective tissue uninvolved by tumor existed between the nodule and the muscularis. Within this connective tissue were numerous small and large vessels. The muscularis underlying the tumor nodule was slightly thickened. One section on microscopic examination disclosed a small focus of tumor unconnected with the main nodule lying immediately external to the muscularis. No other foci of tumor were discernible. Although early investigators (3, 6) regarded the carcinoid as a benign tumor, more recent workers (8, 9) have recognized the malignant character of some of these tumors. Raiford has stated that carcinoids situated in the stomach or colon are more likely to be malignant. The tumor described in this report probably should be regarded as malignant since a small nest of cells was encountered external to the muscularis. However, the cytological features did not differ in any way from those of a benign carcinoid.

Although Wyatt stated that carcinoids do not occur in the rectum, 6 cases including the present one have now been reported in this location.

The generally accepted opinion is that the carcinoid is derived from the Kultschitzky

cells of the mucosa of the intestine. Since Pessin has described these cells as occurring occasionally in the large intestine, carcinoid tumors might be expected to occur in this location. It is entirely possible that in some instances the carcinoid tumor has been confused with the carcinoma in this particular location.

CONCLUSIONS

1. The adenoma is the most common polyp of the large intestine.

2. The most frequent site of the occurrence of adenoma in the large intestine is the sigmoid colon.

3. The second most frequent polyp of the large intestine is the lipoma.

4. The most common sites in the large intestine of the lipoma are the cecum and ascending colon.

5. The leiomyoma is an uncommon tumor of the large intestine.

6. Carcinoids of the large intestine are infrequent. A carcinoid of the rectum is recorded.

REFERENCES

1. Ashworth, C. T. and Wallace, S. A. Arch. Path., Chic., 1941, 32: 272.
2. Comfort, M. W. Surg. Gyn. Obst., 1931, 52: 101.
3. Forbus, W. D. Bull. Johns Hopkins Hosp., 1925, 37: 130.
4. Golden, T., and Stout, A. P. Surg. Gyn. Obst., 1941, 73: 784.
5. Lawrence, J. C. Am. J. Surg., 1936, 31: 499.
6. Oberndorfer, S. Frankf. Zschr. Path., 1907, 1: 426.
7. Pessin, S. B. Arch. Path., Chic., 1931, 11: 171.
8. Porter, J. E., and Whelan, C. S. Am. J. Cancer, 1939, 36: 343.
9. Raiford, T. S. Am. J. Cancer, 1933, 18: 803.
10. Saint, J. H. Brit. J. Surg., 1927, 15: 99.
11. Staemmler, M., Das Lipom. In: Reichel und Staemmler: Die Neubildungen des Darmes. Part 1, pp. 273–279. Stuttgart: Enke, 1924.
12. Stetten, D. Surg. Gyn. Obst., 1909, 9: 156.
13. Stewart, M. J. Lancet, Lond., 1931, 2: 669.
14. Susman, W. J. Path. Bact., Lond., 1932, 35: 29.
15. Swinton, N. W., and Warren, S. J. Am. M. Ass., 1939, 113: 1927.
16. Wyatt, T. E. Ann. Surg., 1938, 107: 260.

CARBAMIDE SULFONAMIDE MIXTURES

Use in Treatment of Compound Fractures and Traumatic Wounds

FREDERIC W. ILFELD, M.D., Major, M.C., U.S.A., Los Angeles, California

IN 1937 Holder and MacKay (4) revived the use of urea (carbamide) in the treatment of infected wounds. Their studies showed that carbamide is relatively harmless to normal tissue, hastens healing, eliminates odor from infected wounds and is bactericidal chiefly by virtue of its solvent action on dead tissue (5). Continuing their studies on wound therapy these authors (6) reported the successful use of a mixture of carbamide (urea) with the sulfonamides (CSM: carbamide sulfonamide-mixture) in 1942. They point out that carbamide enhances the action of the sulfonamides in several ways: (a) tends to rid the wound of certain sulfonamide inhibitors such as pus, débris, and autolytic products; (b) increases the concentration of sulfonamides by increasing their solubility; (c) prevents caking of the sulfa drugs thus lessening their foreign body reaction; and (d) by its hypertonicity in higher concentrations leads to diapedesis and an increase in active cellular defense reaction. One of the principal functions of the drug is chemical débridement of the wound. (Carbamide is inexpensive, usually costing less than 10 dollars per 100 pounds.) After many trials with various combinations, the mixture now used most frequently consists of carbamide (urea) 85 per cent, sulfanilamide 13 per cent, and sulfathiazole 2 per cent. This combination was arrived at on the basis of potential solubility.

Further studies carried out by a group at the University of Minnesota substantiate these findings (12). In one of their experiments 29 cases of bilaterally infected dermatoses were selected for treatment. To one lesion, sulfathiazole alone was applied while the corresponding area on the opposite side was dressed with carbamide sulfathiazole mixture. In each instance the latter area healed more rapidly. From this study they concluded that the effect was due to enhancement of the sulfathiazole action by the urea, to neutralization, or removal of its inhibitors (15).

During the past 14 months a series of 41 patients with compound fractures and other serious traumatic injuries have been treated with carbamide sulfonamide mixtures. These cases have afforded an opportunity to study the clinical use of this combination of drugs. In several instances internal fixation with the Townsend and Gilfillan bone plate (13) and in one instance with steel wire (fracture of olecranon) was necessary. The definitive treatment of compound fractures, tendon and other traumatic injuries herewith described is *intended for use only in hospitals where sufficient time and material, as well as technical skill, is available.* Under these conditions the use of carbamide sulfonamide mixture, internal fixation of the fracture, and primary closure of the wound will result in primary healing.

METHOD

Emergency treatment. The emergency treatment of compound fractures and soft tissue wounds is very simple and can be applied by any one trained in first aid. It consists of sprinkling carbamide sulfonamide mixture in powder form over the wound followed by dry dressing and an elastic or Ace bandage. Fractures are splinted.

Presurgical therapy. Appropriate measures are used to combat shock. These include morphine, oxygen, bed rest, heat, intravenous fluids, blood plasma, and transfusions. Following recovery from shock which usually occurs within a few hours, the patient is taken to the operating room where definitive treatment is performed.

Surgery. The part is prepared by scrubbing the skin with soap and water, gauze sponges

78th General Hospital, Camp White, Medford, Oregon.

being used. The wound itself is cleansed with sterile sponges or cotton pledgets wet with sterile normal saline solution. The whole area is scrubbed for 20 minutes by the clock, the solution of soap and water being changed several times during the process. The skin may be prepared further with ether and tincture of mercresin or merthiolate. No antiseptic is used in the wound. This procedure is carried out by the surgeon or his assistant. Only thoroughly trained personnel should be entrusted with its responsibility.

After the wound is draped with sterile sheets it is irrigated with 1000 cubic centimeters of normal saline followed by 500 cubic centimeters of a saturated solution of carbamide sulfonamide mixture in sterile water; Asepto syringes or an overhead tank with rubber tubing and a glass nozzle are used for this purpose.

Careful and thorough débridement of the wound is then carried out under strict aseptic conditions. The procedure consists of excising about ¼ to ⅛ of an inch of skin around the edges of the wound and removal of all necrotic or injured fat, muscle, or fascia. The amount of tissue taken out is determined by its color, ability to bleed, contractability of muscle, and general appearance (16). Loose fragments of contaminated bone and periosteum are removed. Those pieces of clean bone attached to periosteum may be left *in situ*. During débridement, and other preparation of the wound, a minimum of suture material is used, plain catgut serving for bleeders. The débridement can be described as a partial excision or saucerization of the wound. Irrigation is then repeated with first a normal saline and then a saturated carbamide sulfonamide mixture solution.

Reduction of the fracture is accomplished by traction. When indicated a bone plate may be employed, the fracture impacted, and the bone screws tightened. Lacerated tendons are approximated, the edges are freshened and by means of silk sutures are then brought together after the method of Bunnell.

The surgical procedure proper having been completed, about 1 to 6 ounces of carbamide sulfonamide mixture powder is sprinkled and packed into every part of the wound, the quantity used depending upon the extent of the lesion. It is important that no area be overlooked. The handle of a Bard-Parker knife, a spoon, or a curette may be used to implant the powder. No attempt is made to close the various layers of the wound. The skin alone is approximated by means of a perpendicular mattress suture of silk.

Immobilization is achieved by either internal fixation or the application of a plaster-of-Paris cast. Since all soldiers have had tetanus toxoid a booster dose of 1 cubic centimeter is routinely given. In some of the more severe injuries a prophylactic injection of 5–10,000 units of gas antitoxin may be administered intramuscularly. Sulfathiazole or sulfanilamide may be given orally for the next 10 days. Some of our patients were given sulfanilamide and some sulfathiazole; however, the latter seems more satisfactory in maintaining an effective blood sulfa-level. Blood sulfa-determinations, red and white cell and differential counts, and urine examinations are made on alternate days. Unless there is evidence of a spreading infection, the wound is left alone and is not inspected until the 7th to the 10th day. Skin sutures are removed after the 10th postoperative day.

COMPOUND FRACTURES RESULTING FROM ORDINARY TRAUMA

Table I illustrates the results of treatment in various types of compound fractures and severe tendon injuries encountered in civilian practice; that is, trauma resulting from automobile accidents, athletics, fighting, etc. The interval between the injury and treatment varied from ½ to 12 hours. All were treated by scrubbing, irrigation, débridement, irrigation, reduction, insertion of carbamide sulfonamide mixture powder and primary closure as has been described. Sixteen wounds healed *per primam* and the 2 others healed with a slight serous discharge but no gross infection. In both of the latter instances the skin was approximated under tension. It is interesting to note that in Case 1 patient incurred his injury while riding a scooter in a barnyard. His wound was contaminated with manure. Healing, however, occurred without infection. The following case, Case 2, may be described

TABLE I.—COMPOUND FRACTURES FROM ORDINARY TRAUMA

Case Age	History	Diagnosis	Interval till surgery	Hospital treatment*	Result
1 24	Riding scooter in stable yard, fell injuring right leg	Compound fracture right tibia; simple fracture fibula	6 hrs.	Steinmann pin, skeletal traction	Primary healing
2 19	Jeep collided with civilian car	Compound fracture right elbow, olecranon and humeral articular surface	7 hrs.	500 c.c. plasma. Insertion of steel wire	Primary healing
3 23	Jeep collided with civilian car	(1) Compound fracture right tibia and fibula; (2) fracture left femur; (3) multiple lacerations of scalp	1½ hrs.	Insertion of T & G bone plate	Minor serous discharge
4 31	Caught right hand in circular buzzsaw	Lacerated wound, splitting middle right finger longitudinally extending dorsum of hand to wrist. Laceration of flexor and extensor tendons	1 hr.	Amputation of finger	Primary healing
5 27	Right index finger cut off with power saw	Compound fracture of middle phalanx, right index finger	1½ hrs.		Minor serous discharge
6 36	Caught right thumb in lock of searchlight	Compound fracture of distal phalanx, right thumb	2 hrs.		Healed *per primam*
7 22	Index finger caught on muzzle of gun	Compound fracture of distal phalanx right index finger	5 hrs.		Primary healing
8 25	Thrown from truck striking wrist and forearm on pavement	Compound fracture right radius and ulna. Simple fracture right navicular	5 hrs.	Later reduction fracture of ulna	Primary healing
9 19	Motorcycle collided with truck	Compound fracture left tibia, Colles' fracture, left. Simple fracture scaphoid, left	6½ hrs.		Primary healing
10 23	Jumped to catch football, landed on extended right great toe	Compound dislocation right great toe	5 hrs.		Primary healing
11 34	Jeep overturned striking left forearm	Compound fracture left radius	12 hrs.		Primary healing
12 21	Struck by auto while crossing street	Compound fracture right tibia, simple fracture right fibula. Laceration of forehead	3 hrs.		Primary healing of wound. Phlebitis of left leg
13 19	Driving car, dozed hit tree	Compound fracture left tibia involving knee joint	2 hrs.	Plaster cast	Primary healing
14 27	Struck left hand against piece of glass on street	Compound fracture proximal phalanx, 4th finger, left, laceration extensor tendons left index, middle and ring fingers	6 hrs.	Plaster cast	Primary healing
15 23	Stumbled, falling striking finger against gun, during drill	Compound fracture middle phalanx left forefinger	3 hrs.	Pin pulp traction	Primary healing
16 25	Jeep overturned driving, blackout, injuring right hand	Severe lacerations dorsal surfaces, 3d, 4th and 5th fingers exposing middle and distal phalanges and interphalangeal joints	½ hr.	Closure of as much of wound as possible	Healed without infection
17 42	Struck by auto with extensive laceration right hand and buttock	Laceration of extensor tendons of 2nd and 3d fingers, brush burn of back of hand	5 hrs.	Tendon repair primary closure	Healed *per primam*
18 23	Caught 4th finger in 155 mm. breech block	Compound fracture of distal phalanx left 4th finger	1½ hrs.		Healed *per primam*

*General treatment as outlined in text.

in detail as an example of fractures ordinarily seen in civilian practice:

The patient, a 19 year old male, was thrown to the pavement from a jeep at 7:00 a.m. on June 9, 1942, as a result of a head-on automobile collision. He was rendered unconscious for 2 hours and was admitted to the hospital in shock. There were multiple abrasions about the forehead, shock, and a compound fracture of the right olecranon involving the elbow joint. The laceration over the site of fracture was about 3 inches long, and this wound communicated with the joint. The fracture was of a transverse comminuted type with a separation of about one-half inch between the fragments. In addition there was a V-shaped vertical fracture through the distal midportion of the trochlea and external condyle of the humerus. There was considerable débris in the wound. The red blood cell count was 4,100,000; white cell count 9,950; and the urine ex-

TABLE II.—COMPOUND FRACTURES FROM GUNSHOT WOUNDS

Case Age	History	Diagnosis	Interval till surgery	Hospital treatment*	Result
19 37	Gunshot wound, hand	Compound fracture			Primary union
20 28	Gunshot wound, left hand	Compound comminuted fracture, proximal phalanx, left forefinger. Severe lacerated wound of hand	3 hrs.	Pin pulp traction	Healed by granulation, minor infection
21 26	Gunshot wound, left knee	Wound, left knee joint. Compound fracture left femur	16 hrs.	55 c.c. saturated carbamide sulfonamide solution into knee joint. Partial wound closure	No infection of knee joint, wounds healed by granulation
22 25	Gunshot wound, middle finger, left	Compound fracture, middle left finger 1st phalanx	4 hrs.		Primary union
23 30	Gunshot wound, left index finger, middle phalanx	Compound fracture, middle phalanx, left index finger	3½ hrs.		Primary healing
24 26	Gunshot wound, right great toe	Compound fracture, right first metatarsal and phalanx	8 hrs.	Treated with urea-sulfonamide powder and vaseline pack. Plaster cast	Primary union except web between great and second toe.
25 21	Gunshot wound, left lower leg	Compound fracture head left fibula	2 hrs.		Primary healing
26 22	Gunshot wound, entering right ankle medially going through joint; wound of exit below lateral malleolus	Compound fracture, tibia cuboid, os calcis, right		Treated at another hospital, débridement, vaseline gauze, plaster, sulfanilamide orally. Developed chronic osteomyelitis, treated with curettement, urea sulfonamide and cast	Wound healed by granulation. Gross infection
27 23	Gunshot wound, entry above right patella through quadriceps pouch and left tibia	Penetrating wound right knee joint. Compound fracture left tibia	3½ hrs.		Both wounds healed *per primam*
28 23	Gunshot wound, pistol, left elbow	Compound fracture left humerus. Laceration of brachial artery. Gunshot wound left elbow		Treated at another hospital, débridement, insertion sulfanilamide, gauze pack, and plaster splints. Transfer to Station Hospital 6 hrs. later, progressive infection of elbow and forearm with gangrene	Gross infection. Guillotine amputation
29 25	Gunshot wound, right foot	Compound fracture right third metatarsal	15 min.	Application of cast	Primary healing
30 23	Gunshot wound, palm	Compound fracture left third metacarpal	3 hrs.	Cast with pulp traction	Primary healing

*General treatment as outlined in text.

amination, normal. On admission 500 cubic centimeters of blood plasma was administered intravenously, the wounds were sprinkled with carbamide-sulfonamide mixture powder, dry dressing and Ace bandage were applied, and the fracture was splinted. At 2:00 p.m. after patient regained consciousness and recovered from shock, formal surgery was done.

Under gas-oxygen-ether anesthesia the wound and elbow were scrubbed with soap and water for 20 minutes followed by irrigation with 1000 cubic centimeters of normal saline and then 500 cubic centimeters of saturated carbamide sulfonamide mixture solution. The skin edges were excised for a distance of one-quarter of an inch and all devitalized fat, muscle, and fascia was removed. Irrigation of the wound was repeated. Two drill holes were then made in the distal fragment and one in the proximal fragment. A piece of stainless steel wire was then passed through one hole and around the proximal fragment under the triceps tendon. A second piece of wire was placed through the other drill hole in the distal fragment and through a hole in the proximal fragment. The fracture was reduced by tightening and twisting the wires drawing the fragments into apposition (Fig. 1). A small loose bone fragment of the external condyle of the humerus was excised. Carbamide sulfonamide mixture powder was sprinkled into the elbow joint and throughout the wound. The skin was approximated with interrupted silk mattress sutures. Dry dressing and an Ace bandage were applied. The arm was immobilized in a wire splint with the elbow flexed to a right angle.

Ten thousand units of gas gangrene antitoxin and a 1 cubic centimeter "booster" dose of tetanus toxoid were injected after operation. One gram of sulfathiazole was given orally four times a day for the next 8 days. Temperature prior to operation was 101 degrees; pulse, 90; and respiration, 20. On the first postoperative day, temperature reached 101.8 degrees, 100 degrees on the second, and 99 degrees on the third, thereafter remaining normal until the 21st postoperative day when there was an elevation of 101 degrees because of a slight upper respiratory infection which subsided after 3 days. When the wound was inspected on the 9th postoperative day it showed healing *per primam*, the splint was removed, and active motion was started. Half of the sutures were removed on the 12th postoperative day and the remainder on the 15th postoperative day. The blood sulfa level on the 6th postoperative day after 15 grams sulfathiazole was 4.3. The red and white blood cell counts and urine examinations were normal throughout the postoperative course. Physical therapy was started on the 16th postoperative day. This consisted of infra-red heat and active exercises, and later the carrying of a 5 pound weight. The patient was discharged from the hospital on the 34th postoperative day with active flexion to 65 degrees, extension of 162 degrees, and normal supination and pronation. There were no complaints of pain in the elbow. The wound healed by primary intention.

COMPOUND FRACTURES RESULTING FROM GUNSHOT WOUNDS

Twelve gunshot wounds are tabulated in Table II. All of these resulted in compound fractures and were incurred principally at close range. The time interval between the accident and operation varied from 15 minutes to 16 hours. Two patients were treated elsewhere and received by transfer several days after injury. Both of these patients had been treated by débridement, sprinkling the wound with sulfanilamide powder, gauze packing, plaster immobilization, and leaving the wound open. One patient had developed a chronic osteomyelitis which eventually healed by packing with carbamide sulfonamide mixture powder and plaster immobilization. In the other patient, the brachial artery had been severed in the antecubital fossa and gross infection had developed. There was inadequate circulation in the arm which may explain the inability of the subsequent combined chemotherapy treatment to control the infection. A guillotine amputation of the arm, proximal to the wound, was done on the 16th day after injury. The wound was treated by means of carbamide sulfonamide mixture and adhesive skin traction and healed rapidly. Eight of the 10 wounds under initial treatment at this hospital healed *per primam*. In 2, the tremendous damage, extensive laceration, and loss of skin and blood supply excluded any hope of primary union—our hope being to save the great toe (Case 24) and the finger (Case 20). Both of these wounds healed by granulation and the digits were preserved. There were 2 instances in which the knee joint was involved; both healed without infection and with good joint motion. In 1 patient, 55 cubic centimeters of saturated carbamide sulfonamide mixture in distilled water was injected into the knee joint after closure of the wound. The following case report will serve as an example of our treatment of gunshot wounds:

A 23 year old soldier, Case 30, was admitted on July 1, 1942, with a gunshot wound of the left hand. A dry dressing and tourniquet were applied at the first aid station. The general physical examination on admission was essentially normal.

There was a stellate wound of entry in the palm of the left hand about 5 centimeters across with a V-shaped wound of exit on the dorsum about 6 centimeters by 8 centimeters. There was much destruction of tissue, a comminuted fracture of the shaft of the third metacarpal bone, and the flexor tendons of the index finger were widely exposed and burned with powder.

Under local novocain block, extensive débridement of the wounds was accomplished. The skin and wounds were washed with soap and water, irrigated with saline, and saturated carbamide sulfonamide mixture solution. The skin edges and devitalized tissue were excised. Two loose fragments of the third metacarpal bone were removed. The tendons were intact but the flexor to the index finger was severely burned. Bleeding vessels were tied with No. 0 catgut. Carbamide sulfonamide mixture powder was liberally sprinkled throughout the wounds. The skin was closed loosely with interrupted silk sutures and a pin was placed through the pulp tip of the third finger for traction. The hand was immobilized in a circular plaster cast from below the elbow to the metacarpophalangeal joints.

The postoperative care included sulfathiazole orally, 1 gram four times a day, a stimulating dose of tetanus toxoid, (1 cubic centimeter) and 10,000 units of gas gangrene antitoxin.

Convalescence was uneventful—temperature reaching 99.8 degrees on the 2d and 5th postoperative days. On admission, the red blood cell count was 4,980,000; white blood cell count, 14,300; polymorphonuclear leucocytes, 77 per cent; and

TABLE III.—SHELL FRAGMENT INJURIES

Case Age	History	Diagnosis	Emergency treatment	Interval till surgery	Hospital treatment*	Result
31 22	Shell fragments, struck in neck and right shoulder	(1) Compound fracture right humerus (2) Penetrating wound of neck	Wounds, sprinkled with carbamide-sulfonamide mixture dry dressing, traction splint, 250 c.c. plasma	11½ hrs.	Insertion T & G bone plate. 2 transfusions	Healed *per primam*
32 24	Shell fragments in right shoulder and left knee	(1) Compound fracture right clavicle (2) Abrasion left knee	Wound sprinkled with carbamide sulfonamide mixture	7½ hrs.	Removal of shell fragment, drain inserted	Healed *per primam*
33 21	Shell fragments in both elbows	(1) Extreme shock; (2) compound fracture left radius, humerus, ulna; (3) compound fracture right radius	1500 c.c. plasma, 500 c.c. transfusion. Wounds sprinkled with carbamide sulfonamide mixture. Fractures splinted	11½ hrs.	90,000 units gas antitoxin x-ray therapy. 7 transfusions	Left healed *per primam*. Right grossly infected
34 24	Shell fragments left hand and both shoulders struck	(1) Compound fracture of left 2d and 3d metacarpals. (2) Complete laceration 2, 3, 4 and portion of 5th extensor tendons; (3) Laceration, extensive of left hand; (4) Laceration right and left shoulders	Wounds sprinkled with carbamide sulfonamide mixture powder and dry dressing applied	6½ hrs.	Suture of tendons	Primary healing
35 25	Shell fragments in leftcheek,shoulder and right hand	(1) Compound fracture 1, 2, 3, metacarpals, right. (2) Laceration extensor tendon, 3d. (3) Multiple lacerations right hand, face and left shoulder	Wounds sprinkled with carbamide sulfonamide mixture powder and dry dressing applied	7½ hrs.	Tendon sutured. Lacerations sutured	Primary healing
36 23	Shell fragments	Wound penetrating right knee joint	Wound sprinkled with carbamide sulfonamide mixture	11½ hrs.	Removal of shell fragment	Primary healing
37 27	Shell fragments both thighs	(1) Extensive wounds both thighs. (2) Laceration left femoral artery	Wounds sprinkled with carbamide sulfonamide mixture, dry dressing, compression bandage. Left leg splinted	11 hrs.	Wounds sprinkled with carbamide sulfonamide mixture, wound left open	Gas gangrene amputation
38	Shell fragments right side of head	Wound, lacerated right parietal region head	Sprinkled with carbamide sulfonamide mixture	6½ hrs.		Primary healing
39 31	Shell fragments left and right thighs	Wound, lacerated extensive left thigh and right thigh	Sprinkled with carbamide sulfonamide mixture	9½ hrs.	Drain inserted not closed	Healed by granulation
40 29	Shell fragments face	Wounds, puncture of face	Sprinkled with carbamide sulfonamide mixture	13 hrs.		Primary healing
41 36	Shell fragments abdomen	Wound, lacerated, of abdomen	Sprinkled with carbamide sulfonamide mixture			Primary healing

*General treatment as outlined in text.

lymphocytes, 23 per cent. The urine was normal, Kahn negative. The blood "sulfa" determination on the 3d postoperative day was 2.5 milligrams per cent; red blood cell count, 4,900,000; white blood cell count, 11,800. Sulfathiazole was discontinued on the 8th postoperative day. Traction and sutures were removed on the 22d postoperative day. The wound had healed *per primam*. Physiotherapy, consisting of whirlpool and active finger exercises was started.

It is recognized that novocain infiltration anesthesia in contaminated wounds is not desirable as well as being a sulfa drug inhibitor. Block anesthesia represents no contraindication so far as we can determine.

SHELL FRAGMENT INJURIES

Our experience with carbamide sulfonamide mixture was limited to the ordinary compound fracture and gunshot wounds until an Howitzer gun explosion occurred which resulted in several typical wartime casualties (Table III). The more important injuries consisted of 2 patients with lacerations of tendons of the hand and compound fractures, 3 compound fractures, 1 complete laceration of the femoral artery and extensive thigh wounds, 4 soft tissue wounds, 1 penetrating wound of the knee joint, and 3 intra-abdominal injuries. One patient with extensive

abdominal injuries died within 12 hours from a secondary renal hemorrhage. All the others survived. These cases illustrate the treatment of compound fractures, tendon injuries, joint, arterial and abdominal wounds, gas gangrene, the value of blood sulfa determinations, and the necessity for frequent blood counts, plasma and blood transfusions. This accident served as an introduction to actual war surgery and the efficiency of carbamide sulfonamide mixture in the treatment of war wounds.

The urgent necessity of having large amounts of plasma ready for immediate use was amply demonstrated. Several patients arrived in extreme shock and the immediate use of plasma undoubtedly saved their lives. For example the blood pressure of one patient could not be recorded on arrival at the hospital; his pulse was not palpable and the heart sounds barely audible. Fifteen hundred cubic centimeters of plasma, 500 cubic centimeters of citrated blood and oxygen were necessary to combat his immediate shock. It is our impression that plasma should be available for use in the first aid station prior to, or during, transfer of patients to a hospital. Although these patients arrived at the hospital 1 to 1½ hours after the accident, operation in the seriously injured, other than the intra-abdominal cases, was delayed many hours until shock had been successfully overcome. Plasma and blood transfusions were used freely. As the patients were received, carbamide sulfonamide mixture was sprinkled over the wounds, and dry dressing, Ace bandage, and splints were applied. The patients were then operated on in the order of the severity of their injury. All received tetanus toxoid in 1 cubic centimeter stimulating doses, oral sulfanilamide or sulfathiazole after operation, with frequent red, white, and differential counts and blood "sulfa" determinations. A typical case history follows:

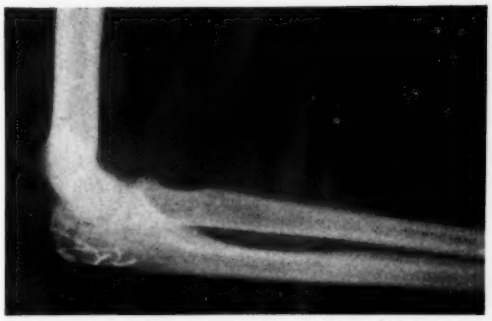


Fig. 1. Case 2. Compound fracture of olecranon and humerus treated with carbamide sulfonamide mixture. Wound healed by primary union.

A 22 year old sergeant, Case 31, was looking up in the air when he was struck in the neck and right

Fig. 2. Case 30. Compound fracture, third metacarpal from .30 caliber gun treated with carbamide sulfonamide mixture. The wound healed by primary union.

Fig. 3. Case 30. Roentgenogram which was made after the compound fracture of the third metacarpal had been reduced.

shoulder by shell fragments. On being hit he was spun around and knocked over. Large amounts of bright red blood were expectorated. There was no pain at all for about 45 minutes.

Upon arrival at the hospital the patient was coughing and raising bright red blood. He was unable to talk above a whisper. There was a laceration on both sides of the neck just above the thyroid cartilage and each wound was about three finger-breadths from the midline. The right side of the neck was tender and swollen; there was no crepitus present; blood was exuding from the nose. On the anterolateral aspect of the right shoulder there was a large ragged wound measuring 6 by 4 inches, involving underlying fascia, deltoid muscle, and extending down into the humerus, which presented a badly comminuted fracture (Fig. 4). There were wounds of entry on the dorsum of the shoulder joint and superior wall of the axilla as well as lacerations in the axilla and posterior aspect of the shoulder. His blood pressure was 118/60; pulse, 128. The remainder of the physical examination was within normal limits.

First aid treatment consisted of sprinkling carbamide-sulfonamide mixture powder on the neck and shoulder wounds, and the application of a dry dressing and bandage. The right arm was immobilized in a Thomas arm traction splint. Two hundred and fifty cubic centimeters of plasma was given intravenously and 1 cubic centimeter of tetanus toxoid subcutaneously. Eight hours after injury, definitive surgery was carried out. Under intravenous pentothal all wounds except those of the neck were cleaned with soap and water and irrigated with normal saline, skin edges and injured tissue were excised and irrigation of the wounds was repeated. The fracture of the humerus was reduced and immobilized with a Townsend and Gilfillan bone plate (Fig. 5). Carbamide sulfonamide mixture powder was dusted into the wound and the skin was closed loosely with interrupted silk sutures without drainage. A fragment of shell in the wound was searched for but not found. The arm was immobilized in a posterior molded plaster splint.

Postoperative care included sulfanilamide orally, 1 gram 6 times a day and intravenous glucose and saline, to maintain the fluid intake. The temperature on the second postoperative day reached 101 degrees, fluctuated between 98.6 and 101 degrees until the 12th postoperative day, thereafter remaining normal. Red blood cell count on the 4th postoperative day was 2,780,000; white cell count, 7,850; sulpha determination, 4.0. On the 4th postoperative day the patient received a transfusion of 500 cubic centimeters of citrated blood. On the 6th postoperative day the red blood cell count was 1,390,000; white cell count, 8,250; and blood sulfa, 5.5. A second transfusion of 500 cubic centimeters of blood was given. The patient was expectorating considerable mucus and had some difficulty in swallowing and talking. The wound on the left side of the neck was healed; that on the right was draining slightly. The shoulder wound was dressed on the 8th postoperative day, and wound healing was *per primam*. On the 10th postoperative day red blood cell count was 3,200,000; white cell count was 12,150; hemoglobin, 9.5 grams; differential polymorphonuclear leucocytes, 69 per cent; lymphocytes, 23 per cent; sulfa determination 5.6 milligrams. Oral sulfanilamide was discontinued on the 14th postoperative day. Sutures were removed on the same day and the wound healed without infection. Due to tension on the skin at the upper portion of the wound, there was slight separation of the skin edges. The plaster splint was removed and the patient was sent to physical therapy department for heat, pendulum, and abduction exercises. The remainder of his convalescence was uneventful. Motions of the shoulder in abduction, flexion, extension, and rotation were normal, and elbow motions were normal. Because the upper portion of the anterior wound was adherent to underlying tissue, this was later excised and resutured. The fracture of the humerus united by bony callus.

EVALUATION

Carbamide sulfonamide mixture when sprinkled over a fresh wound tends to inhibit the growth of bacteria and chemically débride devitalized tissue. In this way when large numbers of casualties are brought in at one time, emergency treatment may be given and patients operated upon in the order of their urgency. In case definitive surgery must be delayed because the patient is in shock or has to be transferred from battalion aid stations to larger installations, the emergency use of carbamide sulfonamide mixture would appear to be most important. When the wound is sprinkled with this powder and dry dressings are applied, surgical operation may be safely delayed and primary closure even attempted long after 6 hours have elapsed.

The danger of using chemicals in traumatic wounds is that the surgeon may err in placing too much reliance on the drug. Baker, in reporting the use of sulfonamides in traumatic and infected wounds, warns that with the use of drugs one is apt to acquire a false sense of security and become lax in following established surgical principles. There is no substitute for thorough and skillful surgery. The surgeon must achieve the gross débridement. Carbamide sulfonamide powder digests necrotic tissue and produces microscopic débridement. It tends to rid the wound of sulfanilamide inhibitors, such as pus, small

Fig. 4. Case 31. Compound fracture of right humerus from shell fragment of 60 millimeter Howitzer, treated with carbamide sulfonamide mixture. Wound healed *per primam*.

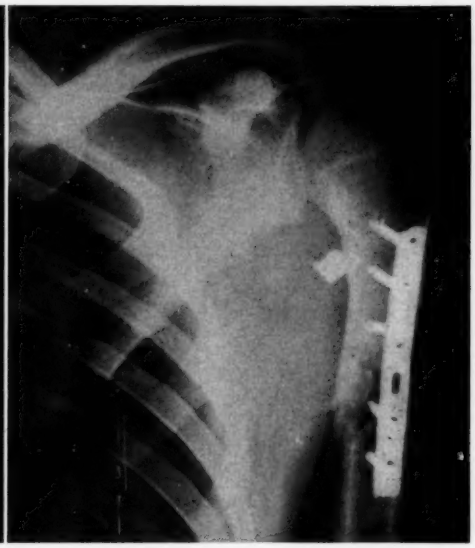


Fig. 5. Case 31. Roentgenogram made after the compound fracture of the right humerus had been reduced and a Townsend-Gilfillan bone plate had been inserted.

débris, and split protein products. The efficiency of sulfanilamide depends on the amount of sulfa inhibitors and also on the amount of sulfanilamide in solution. The carbamide increases the solubility of sulfanilamide and renders the drug about ten times more effective. The carbamide sulfonamide powder causes no burning or sensation of pain when applied to the wound.

The primary closure of contaminated traumatic wounds, particularly those involving fractures, is a question about which there is considerable difference of opinion. Whether or not it is attempted must depend upon the nature of the wound, facilities and circumstances, as well as the skill of the surgeon. The experience of war surgeons dictates that actual war wounds should never be closed by primary suture but packed open loosely. Key (9) referring particularly to compound fractures states that it has been his custom to close such wounds by primary suture after a careful débridement and expect primary healing. By the use of sulfanilamide or sulfathiazole in the wound, or a mixture of the two, he points out that a wound can be sutured with more assurance than formerly and points to the experience of himself (10) and others (7, 8). We believe that the carbamide sulfonamide preparation is an improvement over any of the sulfonamides used in mixtures or alone. It is obvious that in the formal treatment of traumatic wounds primary closure after satisfactory wound hygiene is advisable whenever possible. To allow a preparation such as carbamide sulfonamide to function, it must be kept in the wound. Leaving the wound open allows the mixture to drain out and therefore diminishes its effectiveness. The 2 cases of gross wound sepsis which received initial treatment with the carbamide sulfonamide mixture method we feel were due to failure to achieve effective débridement of the wound.

In Case 37 effective débridement was not possible since the thigh wound was extensive and the muscle so severely contused that removal of all injured tissue was impossible. This wound was covered with carbamide sulfonamide mixture, vaseline gauze, dry dressing, and Ace bandage. The skin was not closed. The femoral artery had been completely severed. Swelling of the leg occurred with subsequent development of gas gangrene. This was our only case

of this type of infection and occurred in a wound in which primary closure was not attempted. The patient received sulfanilamide orally and parenterally. His blood sulfa level was 12 milligrams per cent when gas infection developed. A successful result was accomplished by guillotine amputation, x-ray therapy, sulfanilamide orally, daily local application of carbamide sulfonamide and 100,000 units of gas gangrene antitoxin intramuscularly. It is not possible to determine which was the most effective of these remedies but it is our impression that amputation, x-ray therapy and local application of the carbamide sulfonamide mixture were the most important. In Case 33 patient had both elbows struck by shell fragments resulting in compound fractures of humerus, olecranon, radius, and destruction of the elbow joint on the left and compound fracture of the radius on the right. The injuries were so serious that one consultant thought amputation necessary. Both wounds were treated by the routine described here. The left, which was the more extensive wound, healed *per primam;* the right developed a gross infection, sutures were removed and the wound thoroughly opened. Using frequent carbamide sulfonamide mixture dressings, irrigation with saturated carbamide sulfonamide mixture solution, the wound healed. It is believed that failure to attain satisfactory healing of the right wound was due to unsatisfactory débridement.

The one other case requiring amputation was in a gunshot wound of the elbow with severance of the brachial artery previously related. In the last war it was said that when the main vessel of a limb is cut and the wound extensive, amputation is almost inevitable. These 2 cases, 1 of the femoral artery and the other the brachial, indicate the truth of this observation.

Cleansing the wound by irrigation with carbamide sulfonamide mixture solution is important and should be thorough. An antiseptic may be applied to the skin but never to the wound. A solution strong enough to kill bacteria will injure tissue cells, thus retarding their natural resistance. Irrigation with large amounts of solution produces a mechanical cleansing and should always be used as an adjunct to surrounding skin preparation. Scrubbing and irrigating require time and are apt to be omitted or performed hastily. Nevertheless they constitute important steps in proper wound hygiene. In several wounds, tissue drains were inserted. This is a compromise between the open and primary closure treatment. Drains, of course, allow the carbamide sulfonamide mixture chemicals to escape and so lessen or diminish their local action. Furthermore, the introduction of air permits the formation of a fluid level, thus preventing contact of the mixture to the whole wound. Drains may also introduce infection; they cause a foreign body reaction and encourage scarring. When immobilization of a fracture is achieved by plaster of Paris, the cast, unless there is elevation of temperature, pain, or swelling, should not be disturbed for several weeks. Windows in the cast are not recommended.

Although this group of patients is small, it may be worth while noting that the incidence of severe infection in 32 compound fractures from injury, gunshot or shell fragments receiving original formal surgery at this hospital is 3.1 per cent and all infections, including those with serous drainage is 15.6 per cent. This compares favorably with those reported by Baker of 10 per cent severe infection, and 19.6 per cent for all infections and Campbell and Smith of 18.1 per cent for all infections.

Primary closure of wounds may be carried out safely when they are under close observation and when facilities are available for the continued observation of the patients. Primary suture should never be done if thorough débridement and effective wound hygiene cannot be accomplished because of the extent of the injury or lack of time. Under these circumstances, the method advocated by Trueta or Orr is recommended. If infection develops after closure, the skin sutures may be removed and the wound treated as an open one without fear of any added complications.

Unless there are definite indications, the dressings should not be disturbed until the 10th postoperative day. Frequent inspection of the wound is apt to lead to complications. It is said that "wound curiosity has filled many graves." Half the skin sutures may be removed on the 10th postoperative day and the other half on the 12th. It is our impression that carbamide sulfonamide mixture, as well as sulfanilamide, slightly delays wound healing and retards epithelization. Urea accelerates granulation tissue formation. At the stage of epithelization necessity for the use of carbamide sulfonamide mixture has passed.

The influence of the treatment which has been outlined here upon the duration of hospitalization is difficult to estimate with any degree of accuracy. However, one receives the impression that in addition to the better functional and cosmetic result of primary closure with this treatment there is at least one-third less disability with corresponding rapid return to duty and reduction in the number of hospital days.

One is justified in raising the question of just how much more advantageous is the use of the carbamide sulfonamide mixture powder than sulfanilamide alone. On experimental and clinical grounds, as detailed here, the carbamide sulfonamide mixtures possess numerous advantages. However, good results have been reported using only sulfanilamide (3, 7, 8, 10) but a careful comparison with the results detailed here suggest that the carbamide sulfonamide mixture is much to be preferred. A careful clinical comparison of the two therapeutic agents is indicated. In the interim it would be difficult to dissuade anyone who has had experience with the carbamide sulfonamide mixture as to its superiority.

SUMMARY

1. The use of carbamide sulfonamide mixtures in the therapy of a series of wounds in 41 patients with compound fractures and other serious traumatic injuries is described.

2. Application of carbamide sulfonamide mixture to fresh contaminated wounds as a first aid measure permits a long delay before definitive surgery.

3. A plan of treatment for formal surgery is outlined. The use of carbamide sulfonamide mixture solution for irrigation and implantation of carbamide sulfonamide mixture powder permitted primary closure and healing of contaminated wounds.

4. Results in groups of compound fractures from ordinary trauma, gunshot wounds, and shell fragment injuries are detailed.

REFERENCES

1. Baker, L. D. J. Bone Surg., 1942, 24: 641.
2. Bunnell, S. J. Bone Surg., 1928, 10: 1.
3. Campbell, W. C., and Smith, H. J. Am. M. Ass., 1941, 117: 672.
4. Holder, H. G., and MacKay, E. M. J. Am. M. Ass., 1937, 108: 1167.
5. Idem. Ann. Surg., 1939, 110: 94.
6. Idem. Mil. Surgeon, 1942, 90: 509.
7. Jackson, R. South. M. J., 1941, 34: 319.
8. Jensen, N. K., Johnsrud, L. W., and Nelson, M. C. Surgery, 1939, 6: 1.
9. Key, J. A. J. Am. M. Ass., 1941, 117: 409.
10. Idem. Nebraska M. J., 1939, 24: 367.
11. Orr, H. W., Wounds and Fractures. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1941.
12. Strakosch, E. A., Clark, W. G., Tsuchiya, H. M., and Teneberg, O. J. Comparison of the effect of topically applied sulfonamides, alone and in combination with urea on infected dermatoses. In press.
13. Townsend, K., and Gilfillan, Charles. Personal communication.
14. Trueta, J. Treatment of War Wounds and Fractures. New York: Paul B. Hoeber, 1940.
15. Tsuchiya, H. M., Tenenberg, D. J., Clark, W. G., and Strakosch, E. A. Proc. Soc. Exp. Biol., N. Y., 1942, 50: 262.
16. War Department. T. M. 8–210, Guide to Therapy for medical officers. P. 4, March 20, 1942.

TUBERCULOSIS OF THE ANKLE JOINT

An End-Result Study of Twenty-Five Cases

S. SVERRE HOUKOM, M.D., Duluth, Minnesota

FROM a review of the recent literature it is apparent that the question of conservative versus surgical treatment of tuberculosis of the ankle joint is not yet settled. W. R. Mitchell, in a recent article in the *British Journal of Surgery*, states his opinion that conservative treatment, i.e. recumbency with a right angle splint, is the treatment of choice in children up to the age of 17 years. For adults in whom conservative treatment has failed he advocates early amputation. He believes that arthrodesing operations serve merely to prolong the period of disability and endanger life by disseminating tuberculosis to other parts of the body. On the other hand, Gainslen and Schneider state that amputation and also death from other forms of tuberculosis are far too frequent because conservative measures are persisted in too long. The duration of conservative treatment in their adult cases terminating favorably was over 4 years. Hanson, in his article, quotes the Sorrels, "We have not seen a single case of cure by conservative treatment of an even moderately severe tuberculosis of the talocrural joint with abscesses and fistula." They advocate astragalectomy for all cases.

In 1917 Humphries and Durham published the first report on the treatment of tuberculosis of the ankle joint at the New York Orthopaedic Hospital. These patients were all treated conservatively and of the 29 cases reported, 23 patients were cured and 6 died. Of the 23 patients cured, 15 had free joint motion, without deformity. In a subsequent paper published by Hibbs in 1930 on the treatment of tuberculous joints by operative fusion, he points out that previous to the first fusion operation for tuberculosis of the ankle in 1923, these patients were all given conservative treatment for a period of 4 to 7 years at the Country Branch of the Hospital. The patients discharged as cured were followed in the clinic, and, from 1 to 10 years after discharge from the hospital, many of the joints began to show unmistakable signs of active disease. In commenting on the previous report by Humphries and Durham, Hibbs expressed the belief that in many of the cases they reported the diagnosis had been inaccurate and the period of observation too short. Accordingly Hibbs advocated more accurate diagnosis by pathological section of material removed from the joint and surgical fusion of all positive cases.

At the New York Orthopaedic Hospital it has been the impression of the attending staff that the results of surgical fusion for tuberculosis of the ankle joint are uniformly good. In an attempt to secure a better evaluation of the end-results, a study was made of the 25 cases of tuberculosis of the ankle joint in patients treated from 1923 to 1938 inclusive. All age groups are included. Two other patients were operated upon during this period but have been excluded because of inadequate follow up.

CLINICAL FINDINGS

The age of onset of symptoms in these 25 patients varied from 14 months to 45 years. The average age at onset was 13½ years. In 15 patients the age at onset of symptoms was less than ten years. Of the remaining ten patients 8 were adults of 20 years of age or older. It is evident, therefore, that both the adult group and the younger age group are well represented.

At the time of the initial examination in the clinic, these patients presented the symptoms and signs usually associated with tuberculosis of the ankle joint. Pain, swelling, fluctuation, increased local heat, muscle spasm, limitation of motion, equinus deformity, sinuses, and a

From the Clinic of the New York Orthopaedic Hospital.
Dr. Houkom was formerly an Anne C. Kane Fellow, New York Orthopaedic Hospital.

a b c d

Fig. 1. Case 1. a, Anteroposterior view, both ankle joints, the left ankle is normal; b, lateral view of right ankle joint; c, lateral view of right ankle, 2 months after fusion; d, lateral view, right ankle, 8 years after operation.

unilateral limp were present in varying degree in the different patients. There were five patients who had, before operation, draining sinuses, and 3 patients with healed sinus scars. The duration of symptoms previous to operation varied from 6 weeks to 26 years, the average duration being 5 years. Twelve of the 25 cases had a duration of less than a year. In the 13 remaining patients the durations varied between 1 and 5 years in the majority of cases.

DIAGNOSIS

A presumptive diagnosis of tuberculosis of the ankle joint was made before operation on clinical, x-ray, and laboratory findings. The x-ray findings are of considerable help in establishing the diagnosis, the important feature being a general decalcification of the bone with an associated well defined joint effusion. The presence of bone atrophy, thinning of the joint space, erosion of the articular cortex, and, in the more advanced cases, actual destruction of the bone are also helpful. These findings are not pathognomonic, but when present should make one strongly suspicious of a tuberculous infection. The presence of an elevated sedimentation rate points to an inflammatory process. The absence of a positive Mantoux test is of value in ruling out tuberculosis, since it is most unusual to have a tuberculous joint in the presence of a negative test.

A positive diagnosis of tuberculosis was established in all cases either by frozen section or by the usual pathological section of material removed at the time of operation. It is felt that this is of great importance in evaluating end-results in any group of tuberculous joints.

PREVIOUS TREATMENT

Various types of treatment had been tried on this group of patients before arthrodesis was performed. Most of this treatment was carried out elsewhere, since at this hospital immediate arthrodesis of a tuberculous joint is recommended unless the general condition contraindicates it. The most common forms of treatment were incision and drainage of abscesses, leg casts, and braces. Incision and drainage was done in 8 cases; in some of the cases this was done two or three times. It is doubtful if this form of treatment is ever indicated in a primary tuberculous infection. It usually leads to fistula formation and the development of secondary infection. In some instances when secondary infection is already established, incision and drainage may be necessary as a temporary measure.

Eight patients wore casts or posterior splints for varying periods of 2 months to 1 year. Ankle braces were worn by 6 patients from 3 months to 2 year periods. Two patients were kept in bed for approximately a year's time. Four patients were treated with adhesive strapping, 1 had the ankle manipulated and another had baking and massage. Four patients had no treatment previous to the arthrodesis. This summary of treatment is not intended to give the impression that conservative treatment in these cases was given an

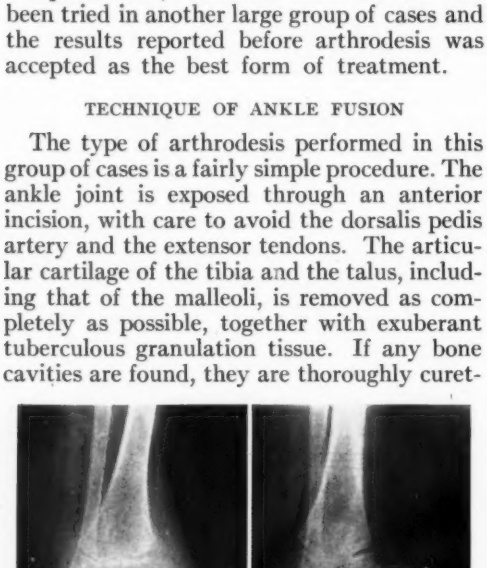
a b c d

Fig. 2. Case 2. a, Anteroposterior view of both ankle joints, the left is normal; b, lateral view of right ankle joint; c, lateral view, right ankle, 2½ years after operation; d, lateral view, right ankle, 13 years after operation.

adequate trial; conservative treatment had been tried in another large group of cases and the results reported before arthrodesis was accepted as the best form of treatment.

TECHNIQUE OF ANKLE FUSION

The type of arthrodesis performed in this group of cases is a fairly simple procedure. The ankle joint is exposed through an anterior incision, with care to avoid the dorsalis pedis artery and the extensor tendons. The articular cartilage of the tibia and the talus, including that of the malleoli, is removed as completely as possible, together with exuberant tuberculous granulation tissue. If any bone cavities are found, they are thoroughly curetted. One must be careful not to damage the distal epiphyseal plate in patients of the younger age group. Following the removal of the articular cartilage, it should be possible to secure apposition of raw bleeding bone surfaces. Bone chips are then removed from the tibial shaft and are jacked into any spaces remaining in the joint and across the anterior aspect of the joint. The wound is closed in layers and a long leg cast is applied, with the foot held in the optimum position of dorsiflexion, usually 100 to 110 degrees.



a b

Fig. 3. Case 3. a, left, Lateral view, right ankle joint; b, lateral view, right ankle, 2 years after operation.

PATHOLOGY

This type of operation affords excellent opportunity for the study of the gross characteristics of tuberculous joint infections. The findings varied with the particular case and the description varied with the surgeon. The joint capsule frequently bulged anteriorly and was thickened and edematous. The synovial membrane was replaced by abundant grayish yellow avascular friable granulation tissue. The articular cartilage frequently was thin, lacked luster, and separated easily from the underlying bone and in some places was completely absent. Cavities in the adjacent bone of the talus or tibia were frequently present and filled with bone débris, caseation or granulation tissue. Cavities were fairly frequent in the head and neck of the talus. In some cases the disease process had extended into adjacent tendon sheaths or had invaded the fossa beneath the talar head and thus by direct extension into the talocalcaneal joint.

PSEUDO ARTHROSIS (FAILURE OF PRIMARY OPERATION)

The experience at this hospital shows that more than one operation may be necessary in tuberculous joints before the arthrodesis becomes solid. This is especially true of the ankle joint because the proximity of the talocalcaneal joint makes involvement of this joint frequent and may necessitate fusion of this joint even though the ankle joint is already fused. In this group 13 patients, or approximately 50 per cent, required only one fusion operation. However, in 16 patients the initial ankle fusion was successful, but 3 of these latter required a fusion of the talocalcaneal joint. Seven patients required two operations, 3 required 3 operations each, and 2 patients required 5 operations each, to secure solid arthrodesis and healthy looking bone.

Of the 12 patients that required more than 1 operation, only 6 of them were less than 6 years of age, which indicates that fusion is not necessarily less successful on the initial attempt in the younger age group. We have 1 patient in whom the first fusion was successful when done at 17 months of age. Five of the 12 patients requiring more than one operation had had incision and drainage of the ankle previous to being treated at the hospital. The establishment of secondary infection with draining sinuses is undoubtedly a factor in the necessity for multiple operations.

In 8 of the 25 cases there was associated involvement of the talocalcaneal joint requiring treatment. One possible unfavorable aspect of the treatment of tuberculosis of the ankle joint by arthrodesis is the chance of dissemination of the infection to the talocalcaneal joint at the time of the ankle fusion. There may be some justification for this idea in 4 of the cases since involvement of the talocalcaneal joint was first noted a year or two after the ankle joint fusion. However, in several instances the talocalcaneal joint was already involved at the time first surgery is attempted. It is felt that conservative treatment would not necessarily cut down the incidence of involvement of this joint, for the longer the disease is allowed to persist the greater the chance for spread to adjacent structures. This is particularly true of the cases in which the talar head and neck are involved. If both the ankle and talocalcaneal joints are involved before surgery is attempted, it is possible to arthrodese both joints at one operation provided there is not too much bone destruction.

POSTOPERATIVE CARE

Following the operation a long leg cast reaching to the mid-thigh is applied. This is left on for 6 weeks following which a walking cast is applied if the condition of the ankle joint permits. The cast is usually kept on until there is x-ray evidence of bony ankylosis. In a few cases after prolonged immobilization the cast was removed when there was clinical evidence of a solid fusion but when the x-ray showed incomplete or only light fusion present. These cases all went on to solid bony union.

If at the end of 7 or 8 months there was unsatisfactory clinical and x-ray evidence of fusion, a refusion was usually carried out. If there was evidence of involvement of the talocalcaneal joint, this joint was usually fused at the same time as the refusion of the ankle. Occasionally the ankle joint went on to ankylosis but the talocalcaneal joint presented evidence of disease, and this joint was fused at varying intervals after the primary ankle joint fusion. The average interval of time between the first and second operation or subsequent operations was 12 months for a refusion of the ankle and 14 months for talocalcaneal fusion, following a primary ankle fusion.

PERIOD OF DISABILITY FOLLOWING OPERATION

The duration of disability in these patients, which means the period of treatment required before free weight bearing was allowed, varied from 3 months to 5 years. The average duration of disability for the 25 cases was 1.2 years, which is considerably shorter than the average period of treatment under a conservative regimen. When conservative methods were used the duration of treatment averaged about 4.7 years and many of these patients when followed for a period of years showed evidence of activity. The period of treatment and disability following surgery does not

necessarily mean hospital care, since most patients, if the progress is satisfactory, can be discharged from the hospital in 3 to 6 months and the cast changed in the clinic as necessary.

ROENTGENOGRAPHIC FEATURES OF TUBERCULOSIS OF THE ANKLE

Some of the characteristic x-ray findings in tuberculosis of the ankle are shown in the accompanying roentgenograms. The x-ray appearance during certain stages of treatment and the final end-result are also shown.

CASE 1. Patient was a girl of 3 years, who had had the disease 1 year. No previous treatment had been given except strapping of the ankle. The anteroposterior view (Fig. 1a) of the right ankle shows definite effusion, bone atrophy, and thinning of the joint space. There is no bone destruction. The opposite normal ankle is shown for comparison. Figure 1b is a lateral view of the right ankle. The joint effusion is more definite and easily visualized. Figure 1c was taken 2 months after fusion. There is less evidence of active infection. The fusion is not yet solid and discreet bone chips are still present. Figure 1d, taken 8 years after operation, when patient was 11 years of age, shows the ankle joint solidly fused. The bone appears healthy; there is no evidence of activity. The epiphyseal line is intact showing that successful fusion can be obtained without interfering with growth. Clinically the patient has an excellent result.

CASE 2. The patient was 3 years of age and the disease, present for 6 months, had been treated with an ankle brace for 3 months. Anteroposterior view (Fig. 2a) of the right ankle shows the characteristic x-ray appearance of tuberculosis. The opposite ankle is normal. Figure 2b is a lateral view of the right ankle showing the marked joint effusion. Figure 2c, a lateral view of right ankle 2½ years after operation, shows that fusion is solid. The bone is healthy and the epiphyseal line is intact. Figure 2d, a lateral view of the right ankle, 13 years after operation when patient was 16 years of age, shows the final end-result with solid fusion and healthy bone. The epiphyseal line has closed.

CASE 3. The patient, 4 years of age, had had the condition 16 months. Previous treatment consisted of incision and drainage shortly after onset. Clinically the patient presented such a severe picture with marked swelling and draining sinuses that amputation was considered. Figure 3a, before operation, shows the marked effusion, with destruction of the superior portion of the talus. Figure 3b, a lateral view, was taken 2 years after fusion. Because of involvement of the talocalcaneal joint, this joint was also fused. Both the ankle and talocalcaneal joints are solidly fused. There is no effusion or soft tissue reaction, although the bone does not yet appear as healthy and contrastable as in previous cases. There is no evidence of activity.

END-RESULTS

In the end-result study of these 25 patients, the follow up period varied from 1½ years to 13½ years, the average follow up period being 6.2 years. An end-result was classified as excellent if it met the following criteria: a solid fusion in good position of 100 to 105 degrees dorsiflexion, no draining sinuses, no swelling or tenderness, no pain either at rest or on weight bearing, normal gait, normal activities, and final roentgenogram showing bony fusion with healthy appearing bone. A result was classified as good if it met all but one or two of the requirements for an excellent result. A result was classified as fair if the fusion was considered doubtful on x-ray examination and a brace considered advisable, although symptoms were slight.

On the basis of outline given, 16, or 64 per cent, of the cases had an excellent result, 6, or 24 per cent, of the cases had a good result, and 3, or 12 per cent, of the cases had a fair result. Combining the excellent and the good results makes a total of 88 per cent satisfactory results. I consider the fair results in this group as being a better end-result than amputation.

In the 9 cases with talocalcaneal joint involvement, the results were excellent in 4, or 44 per cent, good in 4, or 44 per cent, and fair in 1 case. Again the percentage of satisfactory results is 88 per cent.

ANALYSIS OF STUDY

These cases were not selected for operation. Every patient with strongly suspected tuberculosis of the ankle joint, with the exception of those having an active lung lesion, was advised to enter the hospital for further observation and treatment. At operation an arthrodesis was done if the frozen section was positive for tuberculosis or if the gross appearance was that of tuberculosis. In the cases in which a frozen section was not done, the routine tissue sections were positive for tuberculosis in all cases.

Some patients in poor general condition were given a preliminary rest period of 4 to 6 months at the Country Branch of the Hospital. One 3½ year old patient came in with a markedly swollen ankle and 6 profusely draining sinuses. The attending surgeon made the

following note. "Treatment is not easy to decide upon. It might be advisable to perform a midleg amputation now in view of the child's poor general condition. The extensive disease in the tarsus will make arthrodesis difficult and questionable." This patient was given 10 months bed rest at the Country Branch of the Hospital, following which both an ankle and a talocalcaneal arthrodesis was done. It is now 5 years since the operation, and the result is classified as excellent.

The general condition of these patients remained good during the period of observation. One patient was transferred to another hospital because of possible pulmonary tuberculosis. This patient also had tuberculosis of the hip joint. There was no evidence in this group of cases that arthrodesing operations were followed by any ill effects or by any further dissemination of tuberculosis to other parts of the body. On the contrary, the results of fusion had a favorable effect on the general health and well being of these patients. Because tuberculosis is a generalized disease, and its total effect on the body is a result of the virulence and severity of the infection plus the resistance offered, it would hardly seem logical that a surgical procedure of this type would have any untoward effects.

I cannot emphasize too strongly the excellent gait that these patients have, following a successful fusion. It is a popular misconception that an ankle fusion results in considerable disability. This is not true if the ankle is fused in a position of approximately 100 degrees dorsiflexion in male patients and 105 degrees dorsiflexion in female patients and a heel elevation used which corresponds to this degree of dorsiflexion. With a proper heel elevation it is not possible to tell from the gait alone that these patients have a stiff ankle.

CONCLUSION

1. Arthrodesis is the treatment of choice for tuberculosis of the ankle and talocalcaneal joint regardless of age. This procedure very often gives an excellent clinical result, without evidence of disability.

2. In younger patients with extensive bone destruction or in poor general condition, a preliminary rest period of 4 to 6 months may be advisable.

3. The average period of disability when this form of treatment is used is much less than when a conservative regimen is followed.

4. Amputation is rarely if ever indicated in the treatment of tuberculosis of the ankle.

REFERENCES

1. Gainslen, F. J., Schneider, C. C. J. Am. M. Ass., 1921, 77: 1168.
2. Hanson, R. Acta orthop. scand., 1935, 6: 285.
3. Hibbs, R. A. J. Bone Surg. 1930, 12: 749.
4. Humphries, R. E., Durham, H. A. J. Am. M. Ass. 1917, 68: 282.
5. Mitchell, W. R. D. Brit. J. Surg., 1940, 28: 109.

SOME MANIFESTATIONS OF REGIONAL ILEITIS OBSERVED SIGMOIDOSCOPICALLY

RAYMOND J. JACKMAN, M.D., and NEWTON D. SMITH, M.D., Rochester, Minnesota

RELATIVELY little attention has been given in the literature to the anorectal findings in cases of regional ileitis. Ever since 1932, when Crohn and his coworkers established regional ileitis as an entity, we have been impressed with the frequency of certain anorectal manifestations of the disease. We reviewed the records of 114 consecutive cases of regional ileitis in which the diagnosis was made by roentgenologic examination and confirmed by exploration and in which sigmoidoscopic examinations were made. The purpose of the review was to note the lesions of the lower part of the bowel which are more or less peculiar to the disease. We found the following conditions to be characteristic: (1) anal abscess and anal fistula, (2) extrarectal mass, (3) anal ulceration and anal contraction. One other condition, ulceration of the lower part of the bowel, was found in a few cases after short circuiting operations.

ANAL ABSCESS AND ANAL FISTULA

Much attention has been called to the tendency to fistulization in regional ileitis; that is, fistulas tend to originate in the involved ileum and terminate in the abdominal wall or an adjacent viscus. In 1938, Penner and Crohn pointed out that this tendency to fistulization also gave rise to anal fistula and that, in many instances, the first clinical manifestation of the disease might be anal abscess or anal fistula. This manifestation might even precede consciousness on the part of the patient that intestinal function was disturbed. Eight, or 14 per cent, of Penner and Crohn's 50 patients had anal fistula.

Thirty-six, 31.6 per cent, of our 114 patients had anal abscess or anal fistula, or they gave a history of having had an operation for anal fistula within a period of 3 years prior to their visit to the Mayo Clinic. This is more than twice the incidence reported by Penner and Crohn, but they pointed out, and we agree, that unless the patient is carefully questioned, past or present existence of the condition may easily be overlooked.

Eight, 7 per cent, of the 114 patients with regional ileitis came to the clinic primarily because of anal fistula. The regional ileitis was so mild that the patient was not conscious of any intestinal disturbance. In 6 of these 8 cases anal fistulectomy was performed without awareness of the regional ileitis being aroused. The regional ileitis was discovered subsequently, within a year or two, when symptoms of the intestinal disturbance appeared. Study of these cases and also of the cases in which operation was performed elsewhere indicates that with increased alertness to the possibility of coexistence of the two conditions, even more cases of regional ileitis could be found among patients whose primary complaint is anal abscess or anal fistula.

EXTRARECTAL MASS

A mass was palpable in the rectovesical or rectouterine space in 20, or 17.5 per cent, of the 114 cases. This mass, of course, represents an involved segment of diseased ileum, perhaps complicated by pelvic peritonitis and diffuse fistulous tracts. An extrarectal or pelvic mass is generally recognized as being a frequent finding in cases of regional ileitis; its presence is mentioned here only for emphasis (1). Recently we studied the nature of extrarectal masses, produced by lesions of the colon or small intestine, in 58 cases. We found that in 29 cases the extrarectal mass was due to carcinoma of the colon. In 26 cases it was due to diverticulitis. In only 3 cases was it due to regional ileitis. Therefore, if all conditions which will produce extrarectal masses are taken into consideration, regional ileitis accounts for only a small percentage.

ANAL ULCERATION AND ANAL CONTRACTION

Considering the nature of the infected ileal content which is transported to the anal region and the vulnerability of the anal crypts to infection, inflammatory reactions aside from abscess and fistula should be common. Nine, 7.8 per cent, of the 114 patients studied had anal ulcerations or anal contracture.

ULCERATION IN LOWER PART OF THE BOWEL AFTER SHORT CIRCUITING OPERATIONS

On sigmoidoscopic examination of 4 patients, 3.5 per cent of the group, 1 to 2 years after short

From the Section on Proctology, Mayo Clinic.

circuiting operations, ulcerations were found in the lower part of the bowel. These operative procedures consisted of some type of short circuiting operation, such as ileosigmoidostomy and resection of the diseased portion of the ileum. On sigmoidoscopic examination from 1 to 2 years later, ulceration of the mucosa of the bowel near the site of ileal anastomosis was observed. The ulcers were 2 to 3 centimeters in diameter, superficial, and had irregular margins. They were solitary in all but 1 case; in this case 2 ulcers were seen on sigmoidoscopic examination. Their presence probably indicates return of the infectious process.

SUMMARY

One hundred fourteen consecutive patients with regional ileitis, all of whom underwent sigmoidoscopic examination, were studied to determine the anorectal manifestations of the disease. Thirty-six patients, 31.6 per cent, had an anal abscess or anal fistula or gave a history of having had an operation for anal fistula. The main complaint of 8 of these 36 patients was anal fistula; the regional ileitis remained undiscovered until a later date. In examination of 17.5 per cent of this group of 114 patients, an extrarectal mass was found. Anal ulceration, or a contracted anal outlet, was found at examination of 7.8 per cent of the patients. Three and five-tenths per cent had ulceration of the lower part of the bowel after short circuiting operations and resection of the diseased portion of the bowel.

INFERENCES

1. An anal abscess or anal fistula is frequently the factor which will bring a patient with regional ileitis to his physician.

2. If the patient is a young adult with any vague intestinal disturbance, the presence of an anal fistula or the history of an abscess or fistula should lead the clinician to investigate the small bowel for regional ileitis.

3. Any patient who has an anal fistula is entitled to a proctoscopic examination and, if abdominal symptoms coexist, to roentgenologic examination of the large and small intestine.

4. Regional ileitis should be considered as a possible cause of any extrarectal mass of undetermined cause.

REFERENCES

1. Buie, L. A., Jackman, R. J., and Vickers, P. M. J. Am. M. Ass., 1941, 117: 167–169.
2. Penner, Abraham, and Crohn, B. B. Ann. Surg. 1938, 108: 867–873.

THE EFFECT OF ESTROGENIC SUBSTANCE UPON UTERINE MOTILITY DURING LATE PREGNANCY

An Analysis of 153 Observations Made with the Lóránd Tocograph

DOUGLAS P. MURPHY, M.D., F.A.C.S., Philadelphia, Pennsylvania

HOW to treat primary uterine inertia satisfactorily continues to be a pressing obstetrical problem. Because the commonly used oxytocic drugs frequently fail to remedy this condition, the study of any substance which has been shown to influence uterine motility would seem to have merit.

Animal experiments have demonstrated that estrogenic material will increase uterine activity and likewise render the pregnant uterus more responsive to the oxytocic principle of the posterior pituitary gland (6). The human uterus also reacts to the administration of estrogens. Patients suffering from gonorrheal vaginitis have experienced uterine cramps following treatment with this material (6); furthermore, obstetricians have reported improved labor following the administration of estrogenic substance to patients suffering from primary inertia (1, 3).

One observer, using external hysterography, has recorded the effect of estrogenic substance upon the human uterus during labor (2). He found that the drug was inconstant in its action. The number of his observations was small, and his evidence that the material had an oxytocic effect was not entirely convincing.

Such observations as these—based upon either subjective, uncontrolled, or inconclusive evidence—suggested a reinvestigation of the oxytocic property of estrogenic substance. For our study it was considered advisable to utilize patients who were not in labor, in order to have a test organ which was relatively quiescent.

MATERIALS AND METHODS

Thirty-nine women residing in two Philadelphia maternity homes were studied. Their uterine activity and reactivity were registered with a Lóránd tocograph (4, 5). With this instrument we secured 153 sets of observations upon the effect of estrogenic substance on the pregnant uterus, and 19 sets of control observations. All of these were made between the 23d week of pregnancy and labor. A set of observations consisted of 2 tocographic tracings of a given individual on the same day.

Estrogenic material was administered in sesame oil. Two preparations of a-estradiol were used. One form, the dipropionic ester of estradiol, was administered in a dose of either 0.5 milligram or 1 milligram; the other form, the nonesterified material (i.e., plain a-estradiol), was given in a dose of 0.354 milligram, which is the molecular equivalent of a dose of 0.5 milligram of estradiol dipropionate.

Eight control observations followed the administration of sesame oil alone and 11 were made upon patients who received neither sesame oil nor estrogenic substance.

The observations were carried out in the following manner. The patient rested upon her bed for 10 minutes. The tocograph was then placed upon her abdomen. Spontaneous uterine activity was recorded for the following 15 minutes. The tocograph was then removed and the drug was administered. Each dose, in 1 cubic centimeter of sesame oil, was injected intramuscularly in the upper arm. After a predetermined interval of time had elapsed, the tocograph was replaced and a 20 minute record of uterine reactivity was made.

The effectiveness of the treatment was measured in terms of its ability to increase, either, (1) the tonus of the uterus; or (2) the frequency, strength, duration, or rhythmicity of the inter-

TABLE I.—INFLUENCE OF DURATION OF PREGNANCY UPON INCIDENCE OF UTERINE RESPONSE TO ESTROGENIC SUBSTANCE

Duration of pregnancy	Observations	Showing responses	
	Number	Number	Per cent
Weeks			
21–24	3	0	0
25–28	6	0	0
29–32	8	2	25
33–36	55	20	36
37–40	81	40	49
Total	153	62	..

From the Gynecean Hospital Institute of Gynecologic Research, Department of Obstetrics and Gynecology, University of Pennsylvania.

Aided in part by a grant from Ciba Pharmaceutical Products, Inc.

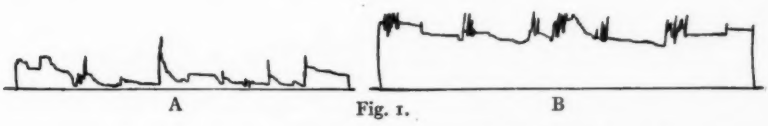


Fig. 1.

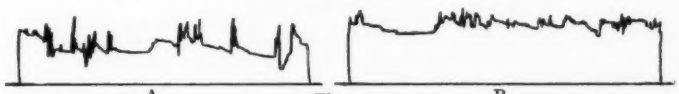


Fig. 2.

Fig. 1. Tracing of uterine motility of patient I. M. secured 6 days before labor. Dose of 0.5 milligram of a-estradiol dipropionate administered at end of tracing A. Note in tracing B that the uterine tonus is very much higher than in tracing A. Vertical strokes in tracing B register active fetal movement. Break between A and B indicates 2½ hour interval.

Fig. 2. Tracing of patient I. M. (Fig. 1) 4 days before labor. Dose of 0.5 milligram of a-estradiol dipropionate administered at end of tracing A. Note the increase in tonus in tracing B, following treatment. This increase occurred although the original tonus was higher than it was 2 days previously (tracing A, Fig. 1). Break in tracing indicates 2½ hour interval.

mittent contractions. The results are presented graphically and statistically.

RESULTS

Of the 153 sets of observations upon the effect of both compounds, 62, or 40 per cent, registered an increase, irrespective of dosage, in one or more characteristics of uterine activity. The a-estradiol dipropionate was administered 112 times in a dose of 0.5 milligram. In 45, or 40 per cent, instances a positive effect was recorded. In 36 cases the a-estradiol dipropionate was administered in a dose of 1.0 milligram. In 15, or 41 per cent, instances a positive response was noted.

The plain a-estradiol was administered 5 times in a dose of 0.354 milligram. A positive response was observed twice, 40 per cent. Therefore, the incidence of uterine response to estrogenic substance appeared to be independent of the form in which the drug was given or its dose.

The 153 sets of observations dealing with the administration of both compounds are summarized in Table I, according to the duration of pregnancy at the time that the treatments were given. No contractile response was observed prior to the 29th week of pregnancy. After the 28th week, the longer the duration of pregnancy, the larger was the number of responses, but at the very end of pregnancy, only about one-half of the tracings recorded a positive response.

The 153 sets of observations are summarized in Table II according to the interval between treatment and the time that observation of uterine reactivity was begun. The positive responses were observed with about equal frequency from 1 to 3 hours after treatment.

Table III records the character of the positive responses. The drug influenced both tonus and the intermittent contractions, the latter slightly more often than the former.

Table IV records the influence of the drug upon the character of the intermittent contractions. The magnitude of all characteristics was increased, especially that of frequency and of strength.

Control observations. The uterine motility of 19 control patients was recorded for a period of 15 minutes, followed by a second record of 20 minutes, at the end of 2 hours. Following their

TABLE II.—INFLUENCE OF INTERVAL BETWEEN INJECTION AND OBSERVATION UPON INCIDENCE OF UTERINE RESPONSE TO ESTROGENIC SUBSTANCE

Interval between injection and observation	Observations	Showing responses	
	Number	Number	Per cent
Hours			
Under 1	4	1	25
1	32	14	44
2	43	18	42
2½	27	11	41
3	31	13	42
4	10	2	20
5	5	3	60
6	1	0	0
Total	153	62	..

TABLE III.—TYPE OF UTERINE RESPONSE TO ESTROGENIC SUBSTANCE

Type of response	Observations	Showing responses	
	Number	Number	Per cent
Contractions	153	51	33
Tonus	153	36	23
Contractions affected and not tonus	153	26	17
Tonus affected and not contractions	153	11	7
Both tonus and contractions	153	25	16

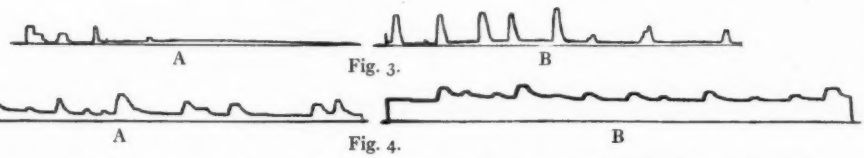


Fig. 3.

Fig. 4.

Fig. 3. Tracing of uterine motility of patient G. J. secured 39 days before labor. Dose of 0.5 milligram of a-estradiol dipropionate administered at end of tracing A. Note in tracing B an increase in the frequency and in the strength of the intermittent contractions, with no accompanying increase in tonus. Break between A and B indicates 2½ hour interval.

Fig. 4. Tracing of uterine motility of patient A. W. secured 8 days before labor. Dose of 0.5 milligram of a-estradiol dipropionate administered at end of tracing A. In tracing B note both an increase in tonus and an improvement in the rhythmicity of the intermittent contractions. Break in tracing between A and B indicates 2½ hour interval.

first tracings, 8 individuals received 1 cubic centimeter of sesame oil containing no estrogenic substance. The remaining 11 patients received no treatment of any kind. In neither group of observations did the second tracing show an increase in activity over that noted in the first tracing.

Graphic observations: Effect primarily upon tonus. Patient I. M. supplied tracings 2,243-A and B, and 2,247-A and B (Figs. 1 and 2). The tracings in Figure 1 were secured 6 days before labor. Immediately following tracing A the patient received 0.5 milligram of a-estradiol dipropionate. Tracing B was started 2½ hours after treatment.

The tracings in Figure 2 were made 4 days before labor. The kind of drug, its dose, and the interval between treatment and observation were the same as for the tracings in Figure 1.

These two sets of observations indicate that an increase in tonus followed treatment, with no appreciable coincident effect upon the character of the intermittent contractions. Increase in tonus is indicated by elevation of the valley level of the intermittent contraction waves above the base line.

Effect upon contractions. Patient G. J., on the 39th day before labor, received 0.5 milligram of a-estradiol dipropionate immediately after tracing 2,204-A was made (Fig. 3). Tracing B was begun 2½ hours after treatment. Note in the second tracing the increase in activity and the change in the pattern of the contractions, which occurred without any appreciable alteration in tonus.

Effect upon tonus and contractions. Patient A. W., on the 9th day before labor, received 0.5 milligram of a-estradiol dipropionate immediately after tracing 2,142-A was made (Fig. 4). Tracing B was begun 2 hours after treatment. Note in the second tracing the concurrent increase in tonus and in rhythmicity of the intermittent contractions.

TABLE IV.—INFLUENCE OF ESTROGENIC SUBSTANCE UPON INTERMITTENT UTERINE CONTRACTIONS

Characteristic of contractions	Observations	Showing responses*	
	Number	Number	Per cent
Frequency	51	45	88
Strength	51	41	80
Duration	51	38	74
Rhythmicity	51	33	64

*Response represented by an increase of the characteristic.

EVALUATION OF STUDY

One value of the present study lies in the fact that it utilized an objective method for recording uterine reactivity. A second value lies in the fact that the tocograph supplies a permanent record which makes it possible to measure the effect of an oxytocic drug quantitatively as well as qualitatively. The third value lies in the fact that our observations were made upon patients who were not in labor. By using them we eliminated the element of strong and variable contractions characteristic of labor, the presence of which has a tendency to overshadow the necessarily weaker contractions induced by an oxytocic drug.

Our observations confirm those of others, namely, that estrogenic substance has an oxytocic effect upon the pregnant uterus. They indicate further that uterine reactivity to the drug is variable, both qualitatively and quantitatively, and that the incidence of response increases as pregnancy advances. Our observations suggest that continued study of estrogenic substance is necessary before its use in the treatment of primary inertia can be placed on a scientific basis.

SUMMARY

1. Estrogenic substance in the form of a-estradiol or a-estradiol dipropionate was administered

intramuscularly to a series of women who were more than 23 weeks pregnant but not in labor. Uterine activity and reactivity were registered with a Lóránd tocograph before and after treatment.

2. The estrogenic substance was variable in its oxytocic effect. No reaction occurred prior to the 29th week of pregnancy. After that time, the number of patients who responded increased progressively as pregnancy advanced. The estrogenic substance increased both uterine tonus and the various characteristics of the uterine contractions, but the nature and degree of the response was unpredictable.

REFERENCES

1. Abarbanel, A. R. Surg. Gyn. Obst., 1941, 73: 257–262.
2. Embrey, M. P. J. Obst. Gyn. Brit. Empire, 1940, 47: 371–390.
3. Jeffcoate, T. N. A. J. Obst. Gyn. Brit. Empire, 1938, 45: 893–917.
4. Lóránd, S. (Loewi). Mschr. Geburtsh. Gyn., 1936, 103: 137–145.
5. Murphy, D. P. Surg. Gyn. Obst., 1941, 73: 681–685.
6. Reynolds, S. R. M. Physiology of the Uterus. New York: Paul B. Hoeber, 1939.

PAPILLARY CYSTADENOMA LYMPHOMATOSUM OF THE PAROTID GLAND

DAVID W. ROBINSON, M.D., and MORRIS S. HARLESS, M.D. Captain, M.C., U.S.A.,
Kansas City, Kansas

A RARE tumor within the substance of salivary glands has been recognized and reported frequently enough within the past 20 years to be known as a distinct pathological entity, although theories of its origin are by no means of uniform accord. The neoplasm has been called adenolymphoma (Jaffe), onkocytoma (Hamperl, Jaffe), and papillary cystadenoma lymphomatosum (Warthin), the latter term being most commonly used at present.

The first case reported was that of Hildebrandt (Freshman and Kurland) in 1898, the author considering the tumor to be of branchiogenic origin. It is highly probable that numerous cervical masses considered branchiogenic cysts have actually been of the type herein reviewed. Warthin, in 1929, reported only 2 cases from several hundred thousand surgical specimens. In 1932, Jaffe had found 21 cases in the literature; Carmichael, Davie, and Stewart, by 1935, collected 26 reported cases and added 8 coming under their own observation; Harris, 1937, reviewed 41 cases, adding 2 of his own; Freshman and Kurland, the following year, stated that they had collected 54 known cases and added another of their own; Tuta and Apfelbach have recently added 1 more; and Plaut, in July, 1942, summarizes 48 cases in the literature and adds 19 more, bringing the total reported to 67.

From the Departments of Pathology and Surgery, University of Kansas Hospitals.

The tumor, itself, is a well encapsulated structure in salivary tissue, usually the parotid, although less frequently the submaxillary, sublingual, or buccal glands. A firm fibrous capsule separates it from the gland itself. The nodular mass is round, oval, coarsely lobulated, or bosselated and is moderately firm but cuts with ease, revealing a cut surface smooth or finely granular with numerous small cystic spaces. These cysts contain a thin serous, milky, or mucilaginous fluid often bearing a fine precipitate.

Histologically, the structure is almost invariably of a well differentiated type, usually quite benign, only 2 of the reported cases showing malignant change. The numerous cystic spaces are lined by two or three layers of pseudostratified columnar epithelium which may be ciliated and thrown up into many broad based branching papillae. In other cases the luminal epithelial layer may be tall, columnar, and nonciliated, while the basilar layer is cuboidal. The stroma consists of a delicate reticulum, sometimes collagenous, in which there are numerous closely packed lymphocytes or follicles with large germinal centers. Examination of the cyst fluid reveals a thick homogenous substance bearing lymphocytes, desquamated epithelial cells, fat globules, and occasional corpora amylacea.

The multiple theories as to the origin of these unusual growths have been well reviewed by Kraissl and Stout, Freshman and Kurland, and

Fig. 1. Case 1. The cystic spaces are lined by a double row of epithelium supported by a lymphoid stroma. The spaces are seen to contain a grumose substance bearing a few lymphocytes. ×80.

Oden. The majority of early authors and many still today consider the cyst of branchiogenic origin. Another popularly accepted belief is the blending of lymphoid tissue of the preauricular node with a parotid lobule, the resulting mixture being separate from the parotid, itself. Warthin, postulated a heterotopia or dystopia of pharyngeal entoderm in or about the parotid, the cells most closely resembling mucosa of the cartilaginous portion of the eustachian tube. Harris speaks of heterotopic salivary gland epithelium in lymphoid tissue. Other theories may be enumerated briefly: (1) failure of extrusion of lymphoid follicles in development of normal salivary tissue; (2) misplaced thymic anlage, (3) ectopic tonsillar inclusion of pharyngeal ectoderm of 3d or 4th branchial pouch; (4) metaplasia of endothelium of lymph vessels or lymphoid embryonic rests; (5) failure of remnants of undifferentiated salivary tissue to fuse with the ductile system; (6) "orbital inclusion," an embryological epithelial structure, the fate of which is unknown in man; and (7), from onkocytes, peculiar epithelial cells of parotid ducts or parenchyma developing in late life, with granular character to the cytoplasm, and with dense, hyperchromatic, and often indented nuclei placed near the lumen.

Papillary cystadenoma lymphomatosa occurs chiefly in men of the 5th and 6th decades. However, the youngest case reported was 2½ years, and the oldest, 92. The occurrence according to sex shows a preponderance of males over females in the ratio of 6:1. The parotid is involved considerably more frequently than any other structure, the two sides showing about equal incidence. The tumor involves most often the lower pole of the parotid, is slow growing, and usually painless unless growth is rapid, and is not attached to the skin, but to the deep structures. According to Carmichael, Davie, and Stewart, the average preoperative duration is 6 years. The growth may vary from 2 to 10 centimeters in diameter. Fungation and ulceration are rare. As the tumor is well encapsulated, it is usually easy to remove. Recurrence is quite rare and irradiation therapy is of no value.

CASE REPORTS

Case 1. J. M., a white male, aged 48 years, was seen in the out-patient department of the University of Kansas Hospitals, May 16, 1941, complaining of right lumbar pain. Incidentally, he mentioned a painless lump of 30 years' duration on his forehead above the eyebrow. It had grown slowly until 4 years ago, increasing in size more rapidly since, but still painless. Within the past 6 months he had a small, hard, nontender mass in his neck just behind the angle of the left jaw.

Examination revealed a firm, lobulated, nontender growth on the left side of the forehead, 2 centimeters in diameter, and 1 centimeter in thickness. It was freely movable, not attached to skin or deep structure. Posterior to the angle of the jaw on the left and in the region of the lower pole of the parotid, there was a firm, round, nontender nodule, 1.5 centimeters in diameter, unattached to the skin, but firmly adherent to deep structures.

Considering the growth on the forehead a firm sebaceous cyst possibly having undergone epitheliomatous change and the cervical nodule, a node probably bearing metastatic carcinoma, both were excised June 7, 1941, under local anesthesia. No difficulty was encountered except that the cervical mass was enclosed in a firm fibrous capsule closely adherent to the parotid capsule. Wounds were healed in 10 days.

The pathological report came as a surprise: On gross inspection, the specimen measured 35 by 17 by 14 millimeters and was covered by a fibrous capsule. A firm area 18 millimeters in diameter was present, but on section this node-like mass revealed a brownish-white cellular structure bearing numerous cystic areas, the largest measuring 4 millimeters in diameter. These spaces contained an amorphous substance having the consistency of cartilage (formalin hardened).

Microscopical study revealed a glandular and in places a papillary-like structure which was lined by a layer of tall cylindrical epithelium. In places, this epithelium was ciliated and now and then appeared to be of an embryonic type. The stroma supporting this epithelium was of the lymphoid type and numerous follicles might be seen, some showing germinal centers. In some of the cyst-like spaces a mucinous secretion was recognized while in others desquamated epithelial cells and clear staining vacuoles were seen. At the periphery of this growth and directly continuous with it there was some salivary tissue with small ductal spaces lined by cuboidal epithelium. Islands of fat cells were scattered throughout the salivary tissue.

The growth removed from the scalp was a typical fibroma durum with areas of osseous metaplasia.

Diagnosis: papillary adenocystoma lymphomatosum of salivary gland, probably parotid; fibroma durum of scalp.

Case 2. R. H., a white male, aged 46 years, was admitted to the University of Kansas Hospitals August 6, 1940, on the service of Dr. T. G. Orr. He stated that 6

Fig. 2. Case 4. The papillary projections of epithelium into cystic lumina. The double row of epithelial cells is clearly demonstrated and the lymphoid stroma is definite. ×110.

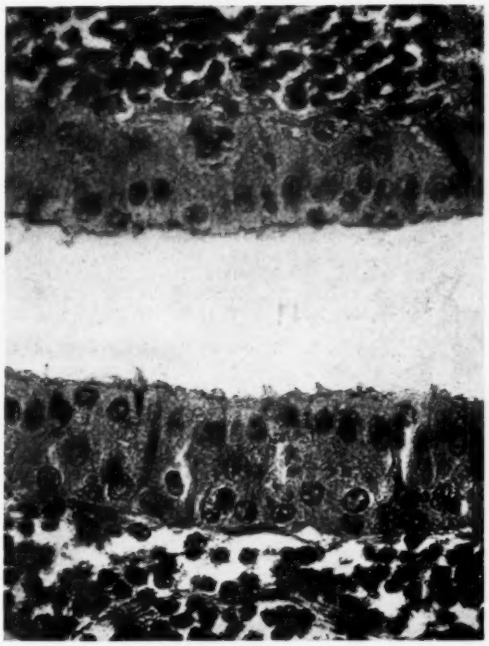


Fig. 3. Case 4. Study of the epithelium shows the luminal columnar and basilar cuboidal layers. A suggestion of cilia may be seen along the luminal border. The basement membrane is fairly definite and lymphocytes in the stroma may be seen. ×550.

weeks before, while shaving, he noticed a small "kernel" just in front of his left ear. It caused him no inconvenience or pain and had enlarged only slightly during the 6 weeks before admission.

On examination, a small tumor, 1.5 by 1 centimeter, was palpable just anterior to the left external auditory canal and extending slightly behind the ascending ramus of the mandible. It was firm, nontender, and movable on all surfaces except deep over the parotid capsule. Clinical diagnosis: parotid tumor.

The mass was excised under local anesthesia, August 7, 1940, without difficulty. It was well encapsulated and deep within the substance of the parotid extending down behind the angle of the jaw in the region of the facial nerve, which was not disturbed.

Grossly, the specimen was spherical, measuring 2.5 by 2 by 1.5 centimeters. It was gray in color with numerous fatty tags on the surface. The mass cut with ease and on cut section the tumor was seen to be cystic with a wall 2 millimeters in thickness. The contained fluid was straw colored. Portions of the inner lining were smooth and glistening, other portions were irregular containing small papillary granulations which extended inward 1 to 2 millimeters.

Section through the wall of the cyst showed a thin fibrous capsule and an inner lining of epithelial structure with papillary processes extending into the lumen. The cells were of indefinite epithelial type and were supported by abundant lymphoid tissue which rested against some glandular duct-like spaces lined by cuboidal epithelium and supported by a small amount of fibrous stroma. An acute and chronic inflammatory reaction was noted in the lymphoid tissue. The sections gave the appearance of some embryonic remnant.

Diagnosis: papillary cystadenoma lymphomatosum of parotid gland.

CASE 3. R. M. G.,[1] a white male, aged 28 years, was admitted March 22, 1937, to the service of Dr. William Ketchum at St. Joseph's Hospital, Kansas City, Missouri, with the chief complaint of weakness and fatigue, worse in the past year. For some time (exact duration not stated) he had had a small lump on the right side of the neck which varied in size and at times throbbed. Examination showed a mass, 3 by 2 centimeters, behind and below the angle of the right jaw fixed to the underlying tissues, but not to the skin. Pulsation was noted and attributed to the underlying vessels. The remainder of the examination, including laboratory procedures, was negative.

Grossly, the mass measured 3 by 2 by 1.5 centimeters and showed a rough fibrous capsule. When it was sectioned it exuded a creamy purulent material which was smeared and cultured; however, it showed no evidence of bacterial organisms.

The histological sections showed a papillary and cystic structure in which the trabeculae were made up of varying thicknesses of fibrous and lymphoid stroma which was covered over by a layer of cylindrical or pavement type of epithelial cells. In some places, the cells were tall columnar in type, while in others they were oval, round, or polyhedral and assumed more of a pavement characteristic, suggesting incompletely differentiated squamous cells. The

[1]Dr. Ketchum kindly permitted us to use this case and Dr. Russel Kerr, pathologist of St. Joseph's Hospital, furnished us with an abstract of his report.

lymphoid tissue was also variable in amount and in some fields actual germinal follicles could be seen. Areas of inflammatory reaction were present with an infiltration of polymorphonuclear leucocytes, some of which were eosinophilic. Desquamated epithelial cells and polymorphonuclear leucocytes could be seen within some of the cystic spaces.

Diagnosis: papillary cystadenoma lymphomatosum of the parotid gland.

CASE 4.[1] A white female, aged 65 years, was seen by Dr. E. H. Dellinger of Las Vegas, New Mexico, in April, 1942. She complained of a growth in the right side of her neck which had been present 3 years, growing slowly. The mass was located lateral to the upper pole of the thyroid on the right just beneath the deep cervical fascia. It seemed completely encapsulated and apparently had no connection with the thyroid itself. The mass was removed in its entirety.

The specimen consisted of several nodular pieces of tissue weighing together 30 grams and the largest measuring 6 centimeters in diameter. The external surface was smooth and resembled serous membrane, with some fibrous tags adherent to the capsule. The tissue was firm in consistency. Cut section revealed a grayish-tan mottled surface, granular and cystic in appearance with irregular foci of yellowish translucent substance. The granular tissue resembled thyroid gland with dilated follicles containing colloid material.

Microscopic examination showed lymphoid tissue supporting numerous irregular anastomosing glandular spaces lined by high, cylindrical epithelial cells with oval or round nuclei near the free edge. In most places, there was a basilar layer of cuboidal epithelium along with the marginal columnar cells, making a double row resting on a thin basement membrane. Some of the columnar cells were ciliated. The lumina of the cystic spaces contained a grumose homogenous substance with an occasional desquamated epithelial cell or lymphocyte. Into the lumina of these glandular spaces, papillary projections of epithelium stood out. Numerous closely packed lymphocytes were present everywhere in the stroma and, in some places, typical germinal follicles were seen. No salivary glandular tissue was seen.

Diagnosis: papilliferous adenocystoma lymphomatosum. Not malignant.

[1]Dr. Dellinger kindly permitted us to use this case report.

With the 4 cases herein reported, 71 have now been described in the literature. These 4 have all been added within the past 5 years from the examination of approximately thirty thousand surgical pathology specimens examined by the pathology department of the University of Kansas School of Medicine and of St. Joseph's Hospital. Since it is only within the past few years, that this tumor has been recognized as occurring in salivary gland tissue, doubtless many new cases will be added to the literature within the next few years instead of being forgotten when classified as branchiogenic cysts or embryonic rests of pharyngeal ectoderm.

The epithelium lining the cysts of the 4 cases reported varied somewhat. All showed the typical two layers of cells, the outer columnar and basilar cuboidal, but Cases 2 and 3 also, showed patchy areas where the epithelium was changing over into a squamous type. Two of the cases showed ciliated columnar epithelium. Warthin's 2 cases had cilia in the lumen of the cysts, but the great majority have not. Nothing to suggest malignancy was noted in our cases. While of a total of 71 now reported, only 2 cases have shown malignant change.

REFERENCES

1. CARMICHAEL, R., DAVIE, T. B., and STEWART, M. J. J. Path. Bact., Lond., 1935, 40: 601.
2. FRESHMAN, A. W., and KURLAND, S. K. Am. J. Clin. Path., 1938, 8: 422.
3. HARRIS, P. N. Am. J. Path., 1937, 13: 81.
4. JAFFE, R. H. Am. J. Cancer, 1932, 16: 1415.
5. KRAISSL, C. J., and STOUT, A. P. Arch. Surg., 1933, 26: 485.
6. ODEN, C. Am. J. Surg., 1935, 30: 57.
7. PLAUT, J. A. Ann. Surg., 1942, 116: 43.
8. TUTA and APFELBACH. Am. J. Surg., 1942, 56: 504.
9. WARTHIN, A. S. J. Cancer Res., 1929, 13: 116.

METASTATIC LESIONS OF THE STERNUM

HARRY B. MACEY, M.D., and GEORGE S. PHALEN, M.D., Rochester, Minnesota

TUMORS involving the sternum are not common. Heuer, in 1932, collected from the literature a total of only 38 cases in which the lesions were reported and described as tumors of the sternum. In this series there were 19 primary sarcomas, 3 so called fibroid tumors, 3 primary cartilaginous tumors, 1 gumma, 1 chronic inflammatory lesion, and 6 metastatic lesions. In the other cases in the series the tumor was not diagnosed. Of the metastatic lesions, 2 were from carcinomas of the breast, 2 from hypernephromas, 1 was from a sarcoma of the breast, and 1 from a "malignant thyroid tumor." Löw-Beer reported 6 cases in which there were destructive lesions of the sternum; in these 6 cases, 2 lesions were metastatic from a carcinoma of the thyroid, 1 was a metastatic lesion from a carcinoma of the breast, 1 was a round cell sarcoma, 1 was a syphilitic lesion, and 1 of the lesions was chronic osteomyelitis with sequestrum.

Of 18 pulsating neoplasms of the sternum reported in the literature up to 1936, Crile concluded that 9 were probably metastatic hypernephromas and 9 were probably metastatic lesions from malignant adenomas of the thyroid. Other cases of pulsating tumors of the sternum secondary to hypernephromas have been recorded by Roth and Davison and by Lewis. In recent years, other cases of sternal tumors have been added to the literature; these include 2 cases of chondrosarcoma (1, 9), 1 gumma (4), 1 neurofibroma (3), 1 echinococcus cyst (11), and an osteomyelitic abscess (7).

In the files of the Mayo Clinic there are 14 cases of neoplastic involvement of the sternum: 4 primary chondrosarcomas, 2 myeloblastic sarcomas, 1 endothelioma, and 7 metastatic tumors. Of the 7 metastatic tumors, 1 is from a carcinoma of the breast, 1 from a carcinoma of the thyroid, 1 from a carcinoma of the stomach, 1 from a carcinoma of the rectum, 1 from a hypernephroma, and 2 are from a possible primary pulmonary malignant lesion. It is with these last 2 cases that we are concerned in this report, since, to our knowledge, no similar cases have been recorded as yet in the literature.

From the Division of Orthopedic Surgery, Mayo Clinic.
Dr. Phalen, Fellow in Orthopedic Surgery, Mayo Foundation.

REPORT OF CASES

CASE 1. The patient, a railroad conductor aged 42 years, was seen at the clinic for the first time on September 22, 1941. He stated that 6 months prior to his coming to the clinic, following the extraction of 2 teeth, he had noticed a gradual onset of pain over the upper third of the sternum. This pain would extend occasionally to the interscapular region and was aggravated by any active forceful movement of the arms. Various medicines and hypodermic injections prescribed by his local physicians had been ineffective in abating the pain, although the pain was lessened to some extent by taking 1 or 2 tablets of acetylsalicylic acid every 2 hours and by complete relaxation of the shoulder muscles. The patient was not seeking compensation although he had been unable to work for 1 month. He stated he would "go back to work tomorrow" if he could be rid of the pain in his chest. He had lost 10 pounds (4.5 kgm.) since the onset of his present illness.

Physical examination gave essentially negative results except for considerable tenderness over the sternum at the level of the 3d and 4th costal cartilages. There was no evidence of swelling, redness, or local elevation of temperature in this region. Results of the flocculation test for syphilis were negative; the concentration of hemoglobin was 12.9 grams per 100 cubic centimeters of blood; leucocytes numbered 9,000, and erythrocytes 4,830,000 in each cubic millimeter of blood. Several urinalyses showed albuminuria grade 1 (on the basis of 1 to 4, in which 1 designates the mildest and 4 the most severe condition), no sugar, an occasional erythrocyte and pyuria grade 2 (30 cells). A roentgenogram of the thorax, taken to show pulmonary detail, was reported as being negative. Roentgenograms of the sternum, however, revealed a destructive lesion involving the body of the sternum with some sclerosis surrounding the lesion (Fig. 1, a and b). From the appearance of the roentgenograms alone, a diagnosis of osteomyelitis of the sternum was made. Roentgenograms of the cervical and thoracic portions of the spinal column were reported as being negative.

It was deemed advisable to remove a specimen of sternal tissue for microscopic diagnosis. At the time of operation, the periosteum of the sternum was found to be greatly thickened; there was no evidence of osteomyelitis; no purulent exudate or abscess cavities were encountered. Microscopic sections of the tissue removed presented the picture of an adenocarcinoma grade 4 (Broders' method), possibly metastatic from a primary pulmonary malignant lesion (Fig. 2).

A course of roentgen therapy was given through four fields converging on the sternum with a moderate voltage technique (130 kilovolts). The total dose was 2,142 r measured in air.

CASE 2. A machinist, aged 41 years, was admitted to the clinic on November 8, 1939. He stated that in February, 1939, he first had noticed the gradual onset of a constant dull pain behind the lower half of his sternum. This pain became progressively worse, with occasional extension to the interscapular region. Coughing aggravated the pain; compression of the chest by strapping with a towel gave some slight relief from pain. The pain was not severe enough to keep the patient awake at night. There had been no dyspnea, hemoptysis, chills, fever, loss of weight

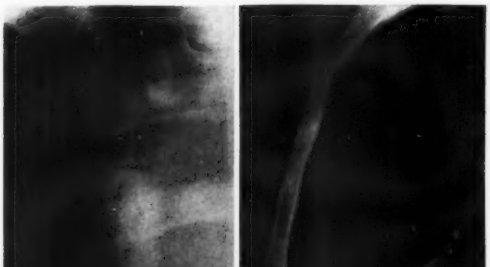


Fig. 1. Metastatic adenocarcinoma of the sternum in Case 1. a, left, Anteroposterior view and b, lateral view, showing a destructive lesion with surrounding sclerosis in the upper portion of the body of the sternum. This has the appearance of osteomyelitis rather than of a metastatic malignant lesion.

weakness, or anorexia. The patient stated that he felt as though he had something behind the sternum that he would like to cough up but his efforts to do so were ineffectual.

In 1937, one week after tonsillectomy, the patient had had an attack of acute polyarthritis involving nearly all the joints except the fingers. The joints were red, tender, and swollen. He was in bed for 3 months, had a high fever and chills, and lost 30 pounds (13.6 kgm.). This condition resolved spontaneously without any apparent residual stiffness of any joint.

On physical examination there was tenderness over the middle third of the sternum with no evidence of swelling, redness or increased warmth. Over the left side of the occiput was a cystic tumor of the scalp approximately 5 centimeters in diameter which had been present since birth; this was believed to be an epidermoid.

Results of the urinalysis and of the flocculation test for syphilis were negative; the concentration of hemoglobin was 15.8 grams per 100 cubic centimeters of blood; leucocytes numbered 12,900 in each cubic millimeter of blood; the sedimentation rate was 4 millimeters in 1 hour. Two examinations of sputum gave negative results for the tubercle bacillus. Roentgenograms of the thorax were reported to show active tuberculosis in the upper lobe of the right lung. Roentgenograms of the skull did not show any involvement of the bone by the soft tissue mass in the occipital region. Roentgenograms of the sternum revealed an extensive destructive lesion of the body of the bone with some proliferative changes (Fig. 3, a and b). The roentgenologist believed that the lesion in the sternum was most likely a neoplastic process.

Several small specimens of tissue were removed from the sternum for diagnosis. At operation it was noted that the lesion seemed to be productive of new bone. Microscopic examination of specimens of tissue removed showed only chronic hyperplastic osteomyelitis with periostitis.

On November 23, 1939, one roentgen treatment was given to the sternum with a moderate voltage technique

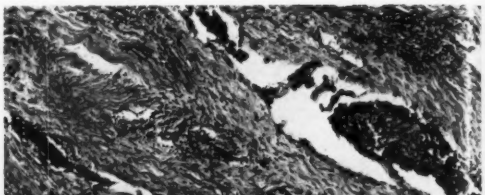


Fig. 2. Specimen removed for biopsy from the sternum in Case 1. Note the large, irregular, anaplastic epithelial cells invading the connective tissue stroma and attempting to form acini.

(130 kilovolts), the dose being 216 r measured in air. The lesion was treated on an inflammatory basis.

The patient returned 3 weeks later to have further roentgen therapy. He stated that for a week after the first treatment he was almost completely free from pain; then there had been a gradual return of the pain. The roentgen treatment given at this time consisted of two converging beams with the same technical factors as used previously, the total dose being 432 r measured in air.

The patient was seen again on January 19, 1940. He had not obtained much relief from the roentgen treatment. Examination of the sputum again gave negative results for fungi and for the tubercle bacillus; the sedimentation rate was 18 millimeters in 1 hour. The results of the first strength purified protein derivative tuberculin test and of the agglutination test for the organisms of brucellosis were negative. Roentgenograms of the sternum showed the same extensive destruction of the body of the bone with proliferative changes as seen in the previous roentgenograms (Fig. 3, a and b). Roentgenograms of the chest also showed little change from those taken on first admission.

The patient died at his home on June 19, 1940. Necropsy was performed by the local physician, and portions of the various organs were sent to Dr. E. T. Bell at the University of Minnesota. Dr. Bell reported on the specimens as follows: "The lung shows adenocarcinoma, and the bone marrow of the sternum is almost entirely replaced by carcinomatous tissue. I am not sure where the primary growth is situated."

In both of these cases there was no palpable or demonstrable tumor mass about the sternum. The chief complaint in each instance was of a constant dull pain over the sternum, occasionally extending to the interscapular region, and the roentgenogram in each case showed a destructive lesion involving the sternal body. In the first case a benign lesion—chronic pyogenic osteomyelitis—was suspected but was disproved by biopsy, while in the second case the original diagnosis of a neoplastic lesion of the sternum was not confirmed by biopsy but was proved at necropsy.

We realize how difficult it is to be certain that the neoplastic lesion of the sternum in these 2 cases was metastatic from a primary pulmonary adenocarcinoma. In Case 1 there was no demonstrable evidence of a primary lesion anywhere in the body; bronchoscopic examination was not performed. The highly malignant and anaplastic character of the cancer cells as seen in the microscopic sections of the specimen taken for biopsy also made it very difficult for the pathologist to state the origin of the tumor definitely; however, the morphological characteristics of the large, irregular epithelial cells, together with their abortive attempts to form acini, make a pathological picture which more closely resembles an adenocarcinoma of the lung than a similar tumor of any other organ.

In retrospect, it is a simple matter to presume that the "active pulmonary tuberculosis" which was diagnosed roentgenologically in Case 2 was in reality a primary carcinoma of the lung. However, the location of the lesion—in the periphery of the upper lobe of the right lung—and the appearance of the lesion in the roentgenogram did not warrant any diagnosis other than pulmonary tuberculosis. Obviously our biopsy of the sternal lesion in this case was not a satisfactory one; tissue representative of the underlying pathological changes was not included in the specimens of tissue removed for microscopic examination. This stresses the importance of securing an adequate biopsy material in every case of a destructive sternal lesion. In this case a second biopsy probably should have been performed, although the course of the disease would certainly not have been altered by an accurate antemortem diagnosis.

If biopsy reveals the presence of a metastatic malignant lesion within the sternum, it is obvious that surgical removal of this bone will neither cure the patient nor prolong his life. On the other hand, if the tumor, benign or malignant, has arisen primarily from the sternum and has not extended too widely, an attempt should be made to remove the lesion in its entirety. This has been done successfully in many cases. Adequate drainage is all that is necessary, as a rule, to heal chronic osteomyelitis with formation of abscess; occasionally it is necessary to remove a large portion of the infected bone. Antisyphilitic treatment is, of course, all that is necessary to cure the rarely encountered sternal gummas.

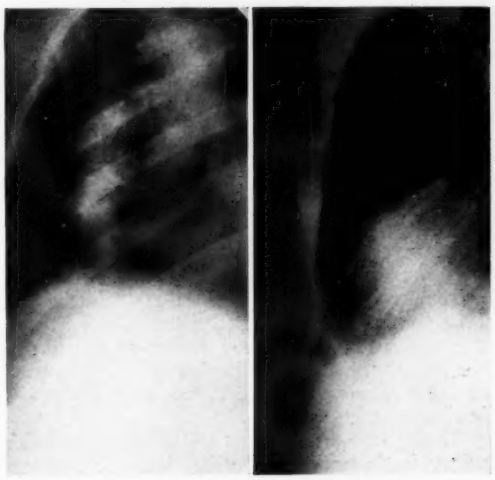


Fig. 3. Metastatic adenocarcinoma of the sternum in Case 2. a, left, Anteroposterior view and, b, lateral view, showing an extensive destructive lesion of the entire body of the sternum with proliferative changes.

SUMMARY

We have presented 2 cases of metastatic malignant lesions involving the sternum and arising possibly from primary pulmonary adenocarcinomas. We wish to stress the importance of taking roentgenograms of the sternum in all cases of sternal pain. If a destructive lesion of the sternum is seen in the roentgenogram, an adequate specimen for biopsy must be taken to determine, first, the benignancy or malignancy of the condition, and second, the feasibility of complete surgical extirpation.

REFERENCES

1. Bradshaw, H. H., and Chodoff, R. J. Am. J. Surg., 1940, 48: 685–687.
2. Crile, George, Jr. Ann. Surg., 1936, 103: 199–209.
3. Gougerot and Meyer-Heine, A. Bull. Soc. fr. derm. syph., 1935, 42: 284–286.
4. Halbron, P., Lenormand, J., Benzaquen, L., and Spire-Weill. Bull. Soc. méd. hôp. Paris, 1933, 49: 1072–1074.
5. Heuer, G. J. Ann. Surg., 1932, 96: 830–842.
6. Lewis, Thomas. Brit. Heart J., 1940, 2: 260–262.
7. Little, G. D. Canad. M. Ass. J., 1936, 34: 185–186.
8. Löw-Beer, Adalbert. Röntgenpraxis, 1931, 3: 817–830.
9. Roberg, O. T., Jr. Surg. Gyn. Obst., 1935, 61: 68–82.
10. Roth, L. J., and Davidson, H. B. J. Urol., 1937, 37: 480–489.
11. Sinberg, S. E. Radiology, 1936, 27: 736–740.

THE CARBON DIOXIDE SNOW ELECTROCAUTERY TECHNIQUE FOR OCCLUSION OF ARTERIES

Suggested Application to Arteriovenous Angioma of the Brain

JUDAH EBIN, M.D., New York, New York

IN an earlier paper (5) a new technique for the occlusion of large venous channels for use in cases in which conventional methods are not adequate has been described. This involves the combined use of carbon dioxide snow and the electrocautery. The application of this procedure to the treatment of venous angioma of the brain has been suggested.

This technique has since been used on arterial vessels in the hope that it might be applied to the treatment of arteriovenous angioma of the brain. In this lesion communication between an artery and a vein has been established by a mass of abnormal vessels which replaces the normal capillary bed. These vessels may be arterial, venous, or both. Cushing and Bailey have described the arteriovenous angioma as a "fairly well circumscribed vascular area composed of manifold, partly thinned and partly thickened vascular trunks forming an inextricable coil of dilated and sinuous vessels of varied caliber through which the arterial blood passes from enlarged entering arteries directly into one or more greatly dilated veins of exit usually with the production of an audible bruit." The lesion lies on the surface of the brain covered by arachnoid and may project deeply into it, in the shape of an inverted cone, abutting on the ventricle. The vascular mass is most frequently encountered in the fields of the middle and posterior cerebral arteries and the artery of the corpus callosum. Increased vascularity of the scalp with large and pulsating arteries, hypertrophy of one or both carotids and even secondary cardiac hypertrophy are frequently met with. The changes in the cardiovascular system are secondary to increased blood volume, which results from the shunting of arterial blood directly into venous channels.

The arterial supply of the lesion originates in surface vessels, although in the fully developed angioma the arteriovenous communication may be deep and thus not visible in the exposed operative field. Two types of arteriovenous angioma as seen at operation may be distinguished. In the first, both the arterial and venous portions of the mass are seen on the surface. The arterial channels are the entering arteries, or a communicating network partly or completely arterial, or both. Venous channels are a communicating network partly or completely venous and terminal veins, or terminal veins alone. In the second, only the venous section of the mass is visible on the surface, the arteries lying beneath it. The venous channels are a purely venous communicating network and terminal veins, or terminal veins alone. The presence of pulsation, thrill and arterial blood distinguishes this type from venous angioma. Histologically, nodular overgrowths of the intima and leiomyomatous nodules in the media have been noted. Hyaline degeneration may occur in the walls of the vessels in any of the coats.

The mode of origin of this lesion is in question. It is generally agreed that it is a congenital blood vessel malformation rather than a new growth. Some believe that it is arteriovenous at first but is not activated until middle life. Others think that it starts as a venous angioma which is subsequently arterialized, perhaps as the result of trauma. Finally, there are those who believe that it may originally be either venous or arteriovenous.

Present methods of therapy include radiation, carotid ligation, decompression, and direct surgical attack. Radiation has not resulted in cure although amelioration of symptoms and signs has been reported. Ligation of the carotid arteries has been of limited value. Butsch and Adson are of the opinion that it should be used only as a last resort in advanced cases. In the presence of marked extracranial vascularity, bilateral external carotid ligation has been done before osteoplastic craniotomy, in order to reduce operative bleeding. Subtemporal decompression and the partial decompression afforded by an osteoplastic flap are beneficial but only temporarily. Permanent relief does not result.

The principal danger in the surgical approach to this lesion is severe bleeding from fragile vessels. The ligature and the electrocautery have been used singly or together. Large vessels have

From the Department of Neurology, Columbia University College of Physicians and Surgeons, and the Neurological Institute of New York.

Fig. 1. An artery, 4.5 millimeters in diameter, frozen and coagulated. a, Normal. *A*, Artery. b, Frozen. c, Application of electrocautery to frozen vessel. *C*, electrocautery. *FA*, frozen segment of vessel. d, Coagulated. *CA*, Coagulated segment of vessel. (Reduced one-sixth.)

been ligated followed by excision of the mass, or by electrocoagulation of the smaller channels; the electrocautery has also been used alone. These methods are hazardous, and severe hemorrhage has not infrequently resulted from their use.

Andrews reported a case in which an excellent result followed the injection of boiling water, homolateral external carotid ligation, and the application of hot soldering iron points. Dandy has presented a series of arteriovenous lesions. In one, very large rolandic and sylvian veins were exposed with a cluster of smaller veins about them. Pulsation of the mass and the presence of arterial blood indicated that there was an arterial communication. Ligatures were placed around the two large vessels, followed by almost immediate rupture of the venous mass between the two ties. In a second lesion, similar to the first, ligatures were placed about the veins, and the cortex was incised in an effort to find the arterial channels. These were located and ligated, following which the mass was removed. Cushing and Bailey reported a case of arteriovenous angioma of the right occipital lobe in which an attempt was made to coagulate the surface of the lesion. Each time the cautery was used a vessel which spurted arterial blood was torn. In Sachs' case the electrocautery was used successfully on the smaller vessels. It was then directed at one of the larger channels. Even though a low current was used, the vessel tore and an extremely severe hemorrhage resulted. Butsch and Adson reported a case in which the entering arteries were ligated and the vascular mass was coagulated with the electrocautery. A similar case was presented by Gardner. Arterial channels were ligated, following which the electrocautery was successfully used on the vascular mass. In Ray's case the electrocautery was used on the angiomatous vessels. The caliber of the vascular channels treated in this manner was greatly diminished, but few vessels were completely occluded.

The carbon dioxide snow electrocautery technique has been used successfully to occlude 6 femoral arteries in dogs. The idea underlying this procedure is identical with that described for venous occlusion (5). Application of a block of carbon dioxide snow with moderate pressure empties and freezes the vessel; the interposed column of blood is eliminated. The apposed walls may then be coagulated by the electrocautery without tearing. The femoral artery in the dog is 4 to 5 millimeters in diameter. Arterial channels in the angiomatous mass of an arteriovenous angioma are seldom larger. As reported previously (5), the inferior vena cava in the cat and the dog have been occluded by the same procedure. These vessels are 6 and 13 millimeters in diameter, respectively. The venous channels of the angiomatous mass and the terminal veins are not of greater size. This procedure may be of use in the treatment of arteriovenous angioma of the brain. The entering arteries might be ligated; the arterial and venous portions of the angiomatous mass and the terminal veins might then be occluded in the manner described.

EQUIPMENT

A complete description of the equipment may be found in the preceding report (5). It includes blocks of carbon dioxide snow, cut with a hack saw, an Allis or curved clamp with rubber tubing on the prongs for handling the refrigerant, and the electrocautery. Both spark-gap and vacuum tube machines were employed in these experiments. These were the Leibel-Flarsheim portable Bovie electrosurgical unit and the Cameron cauteradio

a b c

Fig. 2. A bleeding artery, 5 millimeters in diameter, frozen and coagulated. a, Normal. *V*, Vein; *A*, artery. b, Bleeding. *T*, Tear; *B*, blood. c, Coagulated. *CA*, Coagulated segment of artery. (Reduced one-sixth.)

model O, respectively. The ball electrode measuring 5 millimeters in diameter was used on the vessels.

TECHNIQUE

The procedure is identical with that described for the occlusion of veins (5). To occlude a segment of artery, a block of carbon dioxide snow 6 by 2 by 2 centimeters is applied to it with moderate pressure; this also freezes lateral branches for a short distance before they enter the vessel. Lateral branches are frozen because it is possible for blood to enter the frozen strip through them by means of anastomoses with branches given off proximal to the frozen segment. After 1 minute the refrigerant is removed. The electrocautery is then passed back and forth over the middle 3 centimeters of the frozen segment until coagulation and a slight degree of carbonization have occurred. Because the walls of arteries are thicker than those of veins, the current control is set at a slightly higher level for arteries, i.e., 3 in the vacuum tube machine and 40 in the spark-gap machine, as compared with 2.5 and 30 to 35, respectively, for veins.

During coagulation the two ends of the frozen segment and its branches are watched, and if blood appears in them coagulation is stopped and the procedure is repeated. Similarly, if blood appears in the lumen during coagulation, while the ends and branches are still frozen, coagulation is stopped. The ends are thawed and the procedure is repeated. The presence of blood in the lumen is the result of incomplete emptying due to insufficient pressure in applying the refrigerant. The blood remaining is frozen and then thawed by the cautery.

If cauterization is carried too far, or is continued in spite of the presence of blood in the lumen, the vessel wall may tear. In that event the segment is refrozen and the area about the tear is coagulated. If the exact location of the laceration is not known, the artery is frozen for 15 seconds and then allowed to thaw until blood oozes from the tear. The segment is then refrozen and the area about the laceration is coagulated.

PATHOLOGY

The effects of low temperature freezing have already been considered in detail (5). The conclusion reached was that low temperature freezing in itself does not injure tissue; what little damage follows refrigeration with dry ice is the result of pressure. The damage to brain tissue is superficial and negligible; veins, unaffected by the pressure involved, are not injured by the application of dry ice.

In order to study the long term effects of freezing an artery, a 1 centimeter strip of the femoral artery in a dog was frozen with moderate pressure for 1 minute. The animal was completely normal during the postoperative period. Examination at the end of 3 weeks showed that the vessel was patent and that there was no sterile reaction or infection. On microscopic examination the only change seen was a slight separation of the fibers of the outer layer of the adventitia.

In order to study the long term effects of freezing and coagulating an artery, a 1 centimeter strip of the femoral artery in a dog was occluded. After operation the animal was normal. After 3 weeks the vessel was re-exposed and was found to be still occluded. Neither rupture nor canalization had

occurred. No evidence of sterile reaction or infection was seen. On cross section the lumen was seen to be completely obliterated. Microscopic examination showed that the vessel wall in all its layers had a hyaline appearance as a result of coagulation.

SUMMARY

The carbon dioxide snow electrocautery technique produces permanent closure of both arteries and veins. The procedure is such as to do little damage to adjacent brain tissue. Application of this method to the treatment of arteriovenous angioma of the brain is suggested.

REFERENCES

1. ANDREWS, E. W. Surg. Clin. Chicago, 1917, 1: 965–969.
2. BUTSCH, W. L., and ADSON, A. W. Surg. Clin. N. America, 1935, 15: 1317–1326.
3. CUSHING, H., and BAILEY, P. Tumors Arising from the Blood Vessels of the Brain. Springfield: Charles C. Thomas, 1928.
4. DANDY, W. E. Arch. Surg., 1928, 17: 190–243.
5. EBIN, J. Surg. Gyn. Obst., 1943, 76: 43.
6. GARDNER, W. J. Surg. Clin. N. America, 1936, 16: 1019–1030.
7. RAY, BRONSON S. Surg. Gyn. Obst., 1941, 73: 615–648.
8. SACHS, E. Diagnosis and Treatment of Brain Tumors. St. Louis: The C. V. Mosby Co., 1931.

TOTAL PNEUMONECTOMY

JULIAN JOHNSON, M.D., D.Sc. (Med.), F.A.C.S., Philadelphia, Pennsylvania

NINE years have passed since there appeared the first report of a successful total pneumonectomy. Since that time the operation has been performed by a large number of surgeons, and the percentage of successful results has been steadily increasing. Yet all too often the general practitioner still considers the operation as too hazardous to contemplate. This idea frequently results in such delay in getting the patient to a thoracic surgeon that an operation may no longer be feasible. On the other hand, it has been found that if total pneumonectomy is done upon patients who are in relatively good condition and are suffering from no other organic disease, the mortality will be reasonably low.

The conditions which commonly require total pneumonectomy are bronchogenic carcinoma and extensive unilateral suppurative disease. The latter is usually bronchiectasis but may be multiple lung abscesses. Pneumonectomy may occasionally be justifiable for pulmonary tuberculosis.

DIAGNOSIS

The early diagnosis of bronchogenic carcinoma depends largely upon the physician having a high index of suspicion. The common picture is that of a man in middle life or over who has a persistent cough of a few weeks' duration. The expectoration of some bloody sputum is highly suggestive. Pain in the chest and loss of weight are usually fairly late signs. It is believed, therefore, that every middle aged person who has an unexplained cough lasting 4 weeks or longer should be examined by x-ray and bronchoscope so that a diagnosis of bronchogenic carcinoma may be made early, before the late signs of pain and weight loss appear.

Occasionally an early carcinoma may produce some bronchial obstruction with resulting atelectasis. Infection in the atelectatic area makes the patient febrile and causes weight loss. The extension of the infection to the pleura causes pain. Thus the patient may have the late signs of bronchogenic carcinoma and yet have a localized operable lesion.

From the Surgical Section of the Hospital of the University of Pennsylvania, Philadelphia.

A large majority of bronchogenic carcinomas are within reach of the bronchoscope. Thus tissue may be removed and a positive diagnosis made by microscopy. When the tumor is in the periphery of the lung and cannot be reached by bronchoscopy, aspiration biopsy frequently will reveal a positive diagnosis. It is felt, however, that, if the x-ray appearance suggests carcinoma, an exploratory thoracotomy should be done even though a positive preoperative diagnosis is not made. Tumors situated in the periphery of the lung frequently produce no symptoms until secondary infection occurs. Occasionally there may be mediastinal metastasis before there is a single sign or symptom. In such cases an early diagnosis is an impossibility unless the tumor is found at an examination made for some other reason. (This was the situation in Case 15.)

Bronchiectasis presents the problem of a complete diagnosis rather than an early one. A patient may have had the disease for years, bringing up large amounts of sputum, and because of this be set aside by his physician as a hopeless pulmonary cripple. On the other hand, careful bronchoscopic observations with complete bronchograms may reveal that the disease is entirely unilateral. If the entire lung is involved on one side and the other is free of disease, pneumonectomy offers a complete cure. Even when there is some bronchiectasis on the other side, pneumonectomy may often be justified since the patient may be greatly improved although not completely cured.

Multiple lung abscesses carry a high mortality by any method of treatment. In the event that only one lung is involved, pneumonectomy offers the greatest chance of cure. It should be resorted to as soon as it becomes apparent that the disease cannot be brought under control by simple drainage.

A complete diagnosis of a patient who is a candidate for pneumonectomy for any reason involves the exclusion of other organic disease. The most important is heart disease since there can be no doubt that the heart is put to a severe test during the course of a pneumonectomy. It is important that one be aware of its condition before considering operation. If the patient has severe cardiac disease the idea of pneumonectomy had probably best be abandoned.

PREOPERATIVE PREPARATION

When a total pneumonectomy is to be done for suppurative disease of the lung it is important that the good lung be as free of infection as possible. Repeated bronchoscopic aspirations and postural drainages may greatly improve the local condition and also the patient's general condition. The bronchoscopist must be the judge of when the good lung is sufficiently free of inflammation to go ahead with the operative procedure. Troublesome secretion during the postoperative period may result in atelectasis and bronchopneumonia. For this reason most patients are subjected to bronchoscopic aspiration a few hours before operation, to decrease the possibility of a spill-over during the operative period.

The usual patient with carcinoma does not have enough sputum to make it a major problem, so that very little preoperative preparation is necessary. However, the patient who has infection behind an obstructing carcinoma presents more of a problem. The bronchoscopist should attempt to free the obstruction to allow drainage of the infected area. If the patient's fever subsides, certainly his chances of surviving a pneumonectomy are increased. In the event that satisfactory drainage cannot be accomplished, one must accept the increased risk of operation in the presence of acute infection or abandon the patient to his well known fate.

It is the custom of a number of surgeons to prepare the patient for pneumonectomy by a preliminary pneumothorax. This is done with the idea of getting the patient accustomed to the changed physiology. In the reported series it was found that pneumothorax was impossible in a number of cases first tried. These patients did well in spite of it so that preoperative pneumothorax was given up thereafter. We are not convinced that it is a helpful procedure.

For the last 2 years it has been our custom to use sulfonamide therapy for at least 24 hours before operation.

ANESTHESIA

The thoracic surgeon asks two things of his anesthetists other than keeping the patient asleep, namely, providing adequate aeration and keeping the bronchial tree free of secretions. It is believed that this can be accomplished most satisfactorily by means of an intratracheal tube. The anesthetist can then insure adequate aeration and be constantly available to aspiråte any secretion which may escape from the diseased lung into the trachea or bronchus during the surgical manipulation.

Whether the anesthetist takes over the patient's respirations entirely is a matter of personal preference. This has usually been done in this series. In several instances the patient did not have a spontaneous respiration for more than 2 hours. In none of these patients have any deleterious effects been observed as the results of this procedure. At times the absence of respiratory movements has been greatly appreciated by the operator.

OPERATIVE TECHNIQUE

When an operation is being carried out in the neighborhood of so many vital structures, it is extremely important that one should have a satisfactory visualization of the operative field. Blind dissection should be avoided whenever possible. The Crafoord incision, removing the major portion of the fifth rib, affords an excellent exposure. With this incision the mediastinal structures can be approached either from front or back, and parietal adhesions over almost any portion of the lung can be cut under direct vision. As the experience of the operator increases perhaps he can work safely through a smaller incision. An incision in the fourth or fifth interspace extending from the posterior axillary line to the midline anteriorly has proved to be quite satisfactory in recent cases. One or two costal cartilages may be cut anteriorly if necessary to give adequate exposure over the apex of the lung. This incision is especially valuable in the patient with suppurative disease with considerable purulent sputum. It is felt that such patients should be placed flat on their backs on the operating table to minimize the spill-over of secretion from the diseased lung into the trachea. The anterior incision in the third interspace has been found to be unsatisfactory if there are extensive adhesions present, especially to the diaphragm.

The individual ligation of the great vessels and the separate closure of the main stem bronchus have now been universally adopted, while mass ligation and the multiple suture methods using a lung tourniquet have been abandoned in most clinics. Either heavy silk or catgut ligatures may be used on the great vessels. The usual custom is to place four ligatures on a great vessel, the middle two being suture ties. These two should be separated sufficiently so that when the vessel is cut between them there is a cuff of about ½ centimeter on either side. If this is impossible the sacrifice should be made on the pulmonary side which may be reinforced with a large hemostat.

Most surgeons close the main stem bronchus by the method described by Rienhoff (7) or

some variation of it. By this method the posterior wall of the bronchus is sutured to the anterior wall by three rows of interrupted silk sutures. Regardless of the method of closure of the bronchus it has been observed in this series that when there was so much infection present that the mediastinal pleura was left open, a temporary bronchial fistula has always followed. On the other hand, when the mediastinal pleura has been tightly closed, a bronchial fistula has never been recognized. It is of considerable interest, therefore, that Flick, who makes a point of closing the mediastinal pleura but who closes the bronchus with a single silk tie, has not had one bronchial fistula develop. The possibility suggests itself, therefore, that the closure of the mediastinal pleura is the important thing and that the bronchus stays closed only until the mediastinum is well walled off. This has been suggested in some of our patients by the expectoration of a little mucopurulent material although no bronchial fistula was recognized.

Whether the chest cavity should be closed with or without drainage depends upon the amount of infection present. If a drain is used, it means that the patient will have an infected pleural cavity which usually must be collapsed by a subsequent thoracoplasty. If the chest is closed without drainage and no infection occurs, the period of convalescence will be greatly reduced. On the other hand, the recent work of Longacre and Johansmann suggests that the emphysema resulting in the remaining lung if thoracoplasty is not done may reach a detrimental degree. It is our feeling, therefore, that in the young patient with bronchiectasis for whom a complete cure is expected, the chest should be drained for fear of infection and a thoracoplasty done to avoid future trouble from emphysema. On the other hand, it is desirable to close the chest without drainage in the patient with carcinoma and thereby avoid the morbidity of the subsequent thoracoplasty. Such patients are older than those operated upon for bronchiectasis and in addition have the constant threat of a recurrence of the carcinoma. Therefore, the period of convalescence should be made as short as possible.

Before the chest wound is closed the second to seventh intercostal nerves have been cut or crushed on several occasions. This may be done easily from the inside of the chest and gives the patient a painless wound during the postoperative period. It is believed that this procedure is especially helpful in elderly patients since it allows them to lie on the side operated upon and thereby avoid the dependent pulmonary congestion which is often so troublesome in these cases. It also allows the patient to cough and is very helpful when postoperative secretion is present.

When the chest is closed without drainage 8 grams of sulfanilamide is placed in the pleural cavity.

POSTOPERATIVE CARE

One must expect to give these patients a great deal of attention during the postoperative period if the mortality rate is to be kept at a minimum. Of utmost importance is the maintenance of adequate aeration. The mediastinal structures must not be allowed to shift to the side not operated upon, thereby compressing the remaining lung. The patient whose chest is closed without drainage should be examined at frequent intervals for deviation of the mediastinum. It may be suspected because of tachycardia or respiratory distress. It may be confirmed by feeling for a shift of the trachea in the neck or for a shift of the apex beat. A portable x-ray examination should be done in case of doubt. Fluid or air should be aspirated at intervals if necessary to maintain the mediastinum in the midline or somewhat over to the side operated upon.

The patient whose chest is closed with drainage should have airtight drainage with a constant suction of about 7 centimeters of water exerted in the pleural cavity. In this way the normal pressure relationships are maintained in the thorax. Over a period of days the mediastinal structures will gradually shift to the side operated upon. The pleural cavity may be reduced in size to 200 to 300 cubic centimeters by the shift of the mediastinum, and the elevation of the diaphragm within a period of about 1 month after pneumonectomy. This usually must be closed by thoracoplasty. However, 3 patients in this group had sufficient mediastinal shift to close the entire cavity without thoracoplasty.

In the patient whose chest is closed without drainage the serum in the pleural cavity clots and contracts, producing considerable shift of the mediastinal structures toward the side operated upon. This change reaches its maximum in about 6 months.

The prevention of postoperative atelectasis in the remaining lung is of the utmost importance. It is essential, therefore, that a free air passage be maintained and that any mucus or purulent material be coughed out. The foot of the bed is usually elevated and the patient turned on the side operated upon for 24 hours. This allows dependent drainage until the patient is well over his anesthesia. Pain was found to be a major problem

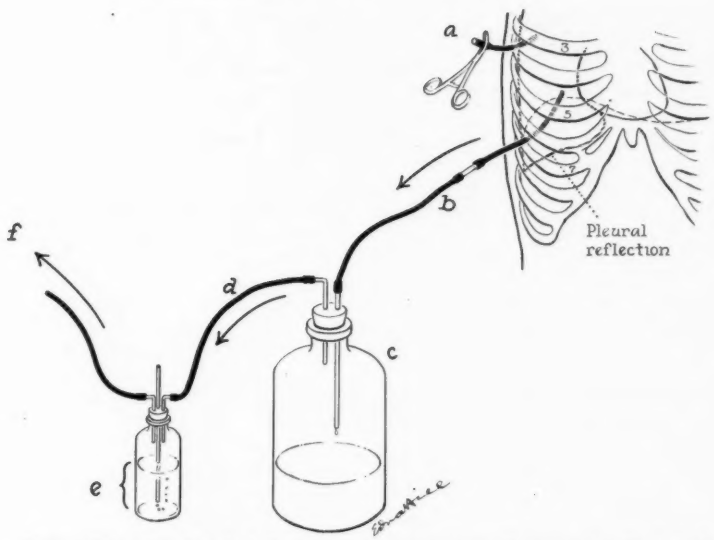


Fig. 1. When the chest is drained after pneumonectomy the apparatus illustrated has been used to maintain negative pressure in the pleural cavity. Continuous water suction is applied at *f*. The amount of negative pressure in the chest is controlled by the depth of the glass tube below the water at *e*. By opening the tube at *a* intermittently, it is possible to maintain a pneumothorax rather than a serothorax and thereby avoid the danger of spill-over into the other lung in the event that the bronchial stump should open.

in some of the patients in whom the intercostal nerves were not cut. It was necessary to find a happy medium in morphine dosage between giving so much morphine that the cough reflex was destroyed, and giving so little that the patient could not cough because of pain. On several occasions it was found necessary to give some morphine before the patient was sufficiently free of pain to cough up the mucus present in the trachea. On the other hand, sufficient morphine to make the patient comfortable, in at least one instance (Case 9), resulted in inadequate coughing and atelectasis of the right upper lobe on the third day after left pneumonectomy. Such a complication seriously threatens a patient's life and may be overcome only by the most energetic treatment.

It has been our experience, therefore, that these patients should be kept lying on the side operated upon, thereby giving good drainage of the remaining lung. The patient must be encouraged to take deep breaths to keep the lung clear and to cough out any mucus or purulent material which may be present. A painless wound due to crushed intercostal nerves has been found to give the patient a tremendous advantage in the execution of this plan.

Oxygen therapy has been used in the form of a nasal catheter for about 3 days after operation. The catheter is preferable to an oxygen tent because it makes nursing simpler and delivers a more constant supply of oxygen. The catheter should be removed and cleaned at frequent intervals. The oxygen tent is frequently used in the summer because of its cooling effect.

In 8 patients the wound was closed without drainage in the hope of shortening the convalescence, although the patients had infection in the lung and were febrile before operation. In spite of intensive drug therapy, infection occurred in all but 1 instance. When infection becomes evident drainage is imperative. This usually means that a subsequent thoracoplasty must be done to collapse the residual empyema cavity. It has been found advisable to wait at least a month after pneumonectomy before doing the thoracoplasty. It is desirable not to wait too long, however, as the pleura may become so thick and scarred that it does not collapse easily. In only 1 instance did infection occur in the serum pocket when the patient had no infection before operation. This case of infection was thought to be due to an inadequate closure of the mediastinal pleura.

Fig. 2. Case 9, 1 year after operation. This roentgenogram illustrates the late shift of the mediastinum when the chest is closed without drainage. The patient now has a fibrothorax on the left. Note the barium in the esophagus with shift of the mediastinum to the left, and elevation of the diaphragm. Also note the enlarged right lung extending over to the left side.

When the chest has been closed without drainage, death may occasionally occur by drowning due to the sudden opening of the bronchial stump with pouring of serum into the remaining lung. To avoid such an occurrence, adequate closure of the mediastinal pleura is advocated. Moreover, the patient is constantly kept on the side operated upon and turned to the back only under supervision. In 2 of our patients whose chest had not been drained (Cases 10 and 14), the wound became infected and a bronchial fistula occurred. In each instance this was recognized and the chest was drained before serious spill-over occurred, probably due to the patient's having been kept on the side operated upon.

If the patient's wound has been closed with a drain to which constant suction has been applied, the chest cavity will still become filled with serum since there is an airtight connection between the tube and chest wall. Thus, if a bronchial fistula should suddenly develop the patient may drown from serum leaking into the trachea. This would be most likely, of course, if he was lying on the side not operated upon and least likely if he was lying on the side operated upon (this almost occurred in Case 11). The danger may be almost completely avoided, by placing a second tube in the chest through which air may be allowed to enter the pleural cavity at intervals, which in turn allows the constant suction to remove the serum from the chest. Thus, a pneumothorax rather than a hydrothorax is maintained on the side operated upon.

MORTALITY

The mortality of total pneumonectomy has been steadily decreasing. It is obvious, however, that it must depend upon the type of patient operated upon and upon the attentiveness to detail in the preoperative and postoperative periods.

The mortality in the young individual should be low whether the operation is for carcinoma or suppurative disease. If, however, the suppurative disease is bilateral the risk is definitely increased. The mortality will of necessity remain fairly high in the group of elderly patients with carcinoma, primarily because of the associated diseases—most common of which is cardiovascular disease. The highest mortality will be found in the group of patients with infection superimposed upon carcinoma.

In the reported group of 20 total pneumonectomies, there was only 1 death. Thirteen of the patients were operated upon for carcinoma, 6 for bronchiectasis, and 1 for multiple lung abscesses. The low average age of the patients in this series undoubtedly is a major factor in the low operative mortality. Nevertheless, this group of patients certainly demonstrates that total pneumonectomy is a relatively safe procedure in the patient without associated complicating diseases.

END-RESULTS

All but 2 of these patients have been operated upon within the last 3 years so that end-results can hardly be reported. It can be said, however, that of the 6 patients operated upon for bronchiectasis having from 300 to 500 cubic centimeters of sputum daily before operation, 3 have apparently been cured and now have no cough and no evidence of bronchiectasis in the remaining lung. The other 3 have been greatly improved but still have occasional expectoration due to minimal bronchiectasis in the other lung. The patient with multiple lung abscesses has been completely cured and has no cough.

Of the 13 patients with bronchogenic carcinoma, 1 died of infection in the hospital, and 2 died of metastasis within a year. Two have now

gone more than 2 years without evidence of metastasis, 2 are well after 1 year and 6 for less than 1 year.

CASE REPORTS

CASE 1. W. H., male, aged 17 years, in whom bronchiectasis was present for 11 years. The patient had repeated bronchoscopic treatments with symptomatic improvement. A bronchogram showed extensive bronchiectasis on the left. There was about 100 to 200 cubic centimeters of sputum daily. A left total pneumonectomy with drainage was done on October 2, 1937. The empyema closed without subsequent thoracoplasty. The patient is now well over 4 years with no cough.

CASE 2. E. M., female, aged 30 years, was found to have bronchiectasis in 1926. A right thoracoplasty was done elsewhere in 1932. She was seen by us in 1937 when she had severe bronchiectasis on the right side. There was about 200 to 300 cubic centimeters of sputum daily. A right total pneumonectomy was done in three stages, removing one lobe at a time by the multiple suture method, the last operation, on October 22, 1938. At her worst she coughs up 30 to 40 cubic centimeters of pus a day. A bronchial fistula was present for months but is now closed.

CASE 3. J. K., male, aged 33 years, had coughed as long as he could remember. He had brought up 300 to 400 cubic centimeters of pus daily for the last 4 or 5 years. A bronchogram was normal on the right, but showed severe bronchiectasis on the left. A total left pneumonectomy with drainage was done on July 5, 1939. Thoracoplasty was performed on August 30, 1939. The patient has been entirely well with no cough since the operation.

CASE 4. E. W., female, aged 26 years, had had productive cough for 10 years. There was hemoptysis at intervals for 3 to 4 years. The daily sputum was about 100 cubic centimeters. An incomplete bronchogram showed bronchiectasis in the left lower lobe. She was first seen by us in severe hemorrhage. A pneumothorax was required to stop it. Without the lung being allowed to re-expand, a left lower lobectomy was done by the multiple suture method on October 21, 1938. The patient still had about 50 cubic centimeters of sputum daily. A bronchogram showed bronchiectasis in the left upper lobe. Therefore, a left upper lobectomy was done on September 6, 1940 by individual ligation without drainage. The bronchus opened but the pleural space was walled off. A thoracoplasty was done after drainage of the cavity. She still has some cough from minimum bronchiectasis in the remaining lung.

CASE 5. M. M., female, aged 36 years, had had a productive cough since a right-sided pneumonia in January, 1939. A bronchogram showed severe bronchiectasis in the right upper and lower lobes. There were several severe hemorrhages. There were about 300 to 400 cubic centimeters of sputum daily. She weighed only 90 pounds, having lost 70 pounds during her illness. A right total pneumonectomy with drainage was done on October 28, 1940, and a thoracoplasty on January 3, 1941. The wound is now closed. She is perfectly well with no cough and has regained her normal weight.

CASE 6. J. P., male, aged 22 years, had had bronchiectasis for about 10 years. When first seen by us in 1939, he coughed up about 500 cubic centimeters of pus daily. Bronchogram showed extensive disease on the left and minimal bronchiectasis on the right. There were frequently periods of fever with a friction rub on the right. After almost 2 years' treatment the sputum was reduced to 200 cubic centimeters a day and the right lung was fairly clean. A left pneumonectomy without drainage was done October 6, 1941. The serum pocket became infected and required drainage. A thoracoplasty was done on January 19, 1942. The patient has very little cough and almost no sputum.

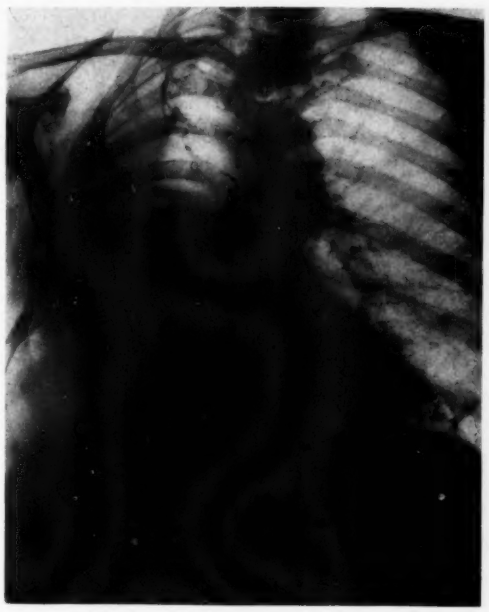


Fig. 3. Case 13, 1 year after operation. This roentgenogram illustrates the closure of a total empyema cavity without the aid of a thoracoplasty. Note barium in the esophagus showing the tremendous shift of the mediastinum which allowed the cavity to close. This case is exceptional in that a thoracoplasty must usually be done to close the cavity.

CASE 7. V. D., female, aged 41 years, had epilepsy for 6 years. The productive cough started in June, 1939. There were several small hemorrhages. She was seen by us in October, 1939, and 2 abscesses were seen by x-ray film in the right upper lobe. These were drained on November 1 and 11, 1939. A third abscess was found in the right middle lobe and drained February 9, 1940. A fourth abscess was found in the right lower lobe and drained on April 17, 1940. The patient continued to be febrile and a fifth abscess was seen by x-ray film. Therefore, a total right pneumonectomy with drainage was done on June 10, 1940. A thoracoplasty was done on September 17, 1940. The patient is now well with no cough. She still has a small draining sinus.

CASE 8. C. L., male, aged 42 years, had had 3 bouts of fever and pain in the left chest, diagnosed as pneumonia, since January, 1936. He was seen by us in January, 1939 with complete atelectasis and infection of the left lung due to a tumor of the left bronchus. He was given x-ray treatment. A bronchoscopic biopsy of this tumor was regarded as a "benign bronchial adenoma." A left total pneumonectomy without drainage was done on March 8, 1939. The surgical specimen was thought to be a spinocellular carcinoma. No metastasis to the lymph nodes was found. The serum pocket became infected and was drained on April 26, 1939. There was evidence of metastasis to the right lung and left femur on May 11, 1939. He died of cerebral metastasis on June 28, 1939.

Fig. 4. Case 14, 6 months after operation. This illustration shows the closure of a total empyema cavity after pneumonectomy by means of a thoracoplasty. Note that mediastinum is only moderately shifted to right side.

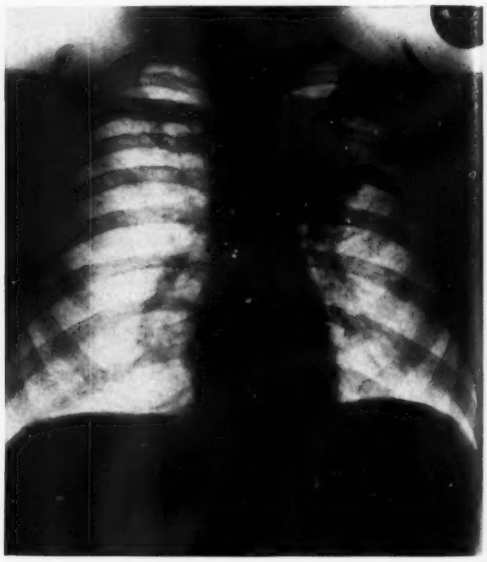


Fig. 5. Case 15 before operation. This picture shows how large a bronchogenic carcinoma may become with absolutely no symptoms. This tumor was known to have been present for 7 months.

Case 9. J. H. N., male, aged 48 years, had a cough with blood-streaked sputum which started in November, 1939. A tumor was removed from the left upper lobe bronchus in December, 1938. It was diagnosed as a "benign bronchial tumor." There was a recurrence of symptoms plus pleural pain in June, 1939. X-ray examination showed atelectasis of a portion of the upper lobe in November, 1939. The tumor could not be seen by bronchoscopy but secretion was seen coming from the left upper lobe. A left total pneumonectomy without drainage was done on November 7, 1939. There was a tumor about 2 centimeters in diameter, and about nine-tenths outside of the bronchus. The surgical specimen was regarded as adenocarcinoma of low grade malignancy. There was no evidence of lymph node metastasis. He has been well for 2 years without evidence of metastasis. The mediastinal shift is marked.

Case 10. A. G., male, aged 31 years, had "grippe" on December 1, 1939. There was blood-streaked sputum on December 13, 1939. X-ray films showed atelectasis of the right lower lobe. Bronchoscopy showed a tumor obstructing the lower lobe but extending up to the bifurcation of the trachea. A right total pneumonectomy was done on January 12, 1940. The microscopic diagnosis was carcinoma of basal cell type of low grade malignancy. The serum pocket became infected and was drained on January 30, 1940. The patient ran a fever off and on and lost considerable weight so that he was never in shape for thoracoplasty until October 4, 1940. He still has a small draining sinus but is well and has regained his normal weight. There is no evidence of metastasis 2 years after operation.

Case 11. D. V., male, aged 39 years, had a cough and blood-streaked sputum which were present on August 8, 1939. In October, 1939, he developed all the signs of pneumonia of the right upper lobe. X-ray film showed complete consolidation of the right upper lobe in December, 1939. Bronchoscopy showed a tumor of the right upper lobe bronchus. It was an adenocarcinoma of grade III malignancy. His temperature rose daily to 102 to 104 degrees F. He was operated upon January 3, 1940. The right upper lobe was hard as in gray hepatization. There were mediastinal metastases. A total right pneumonectomy was done as a matter of expediency and 4 or 5 metastatic nodes removed from the mediastinum. The chest was closed with drainage. The patient was greatly improved and was free from fever for the rest of his life. The wound was closed without thoracoplasty. The patient died of metastasis on September 1, 1940.

Case 12. F. G., male, aged 40 years, had had a lung abscess behind a carcinoma for 3 months when first seen by us in September, 1940. He had lost weight from 210 to 155 pounds. His temperature rose to 102 to 104 degrees daily. The tumor was an undifferentiated carcinoma. He was operated upon on October 2, 1940. Gross pus spilled in separating the adhesions to get to the mediastinum. Metastases were found in the mediastinal lymph nodes. Because of the gross contamination of the pleura a total left pneumonectomy was done as a matter of expediency. The chest was closed with drainage. The patient developed overwhelming infection and died of septicemia on the 18th postoperative day.

Case 13. C. H., male, aged 55 years, in whom weakness was present for 1 year. There was blood-streaked sputum in November, 1940, and a cough developed since then. There was a low grade fever. X-ray film showed atelectasis of part of the right upper lobe. Bronchoscopy showed a tumor of the right upper lobe bronchus extending into the right main stem bronchus. A right total pneumonectomy without drainage was done on February 3, 1941. The

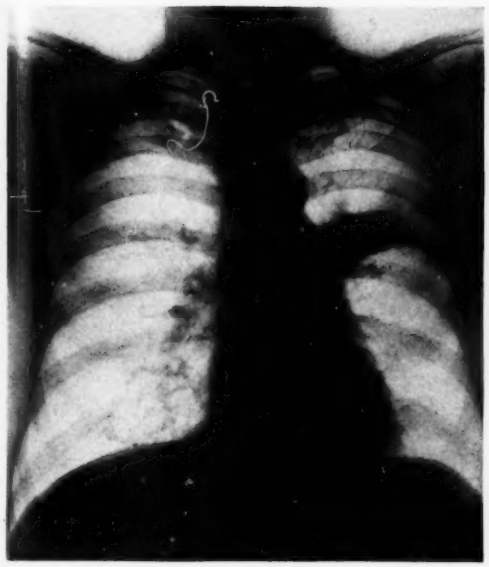


Fig. 6. Case 16 before operation. This roentgenogram illustrates that a small lesion may produce symptoms early. The lesion shown in the x-ray film was due mainly to atelectasis. The tumor obstructing the branch bronchus was only about 5 millimeters in diameter.

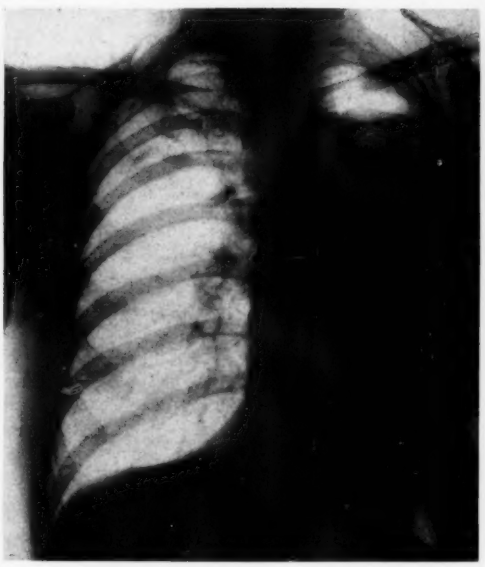


Fig. 7. Case 17, 1 month after operation. This film illustrates that the mediastinum may not be shifted very much soon after operation. The chest cavity had not yet become completely filled with serum. As the serum clots and is absorbed the mediastinal shift gradually increases.

tumor was an undifferentiated carcinoma of grade III malignancy. No metastasis was seen in the lymph nodes. The serum pocket was drained because of infection on February 14, 1941. The mediastinum came over enough in about 4 months to close the pleural cavity without a thoracoplasty. The patient is now apparently well.

CASE 14. C. Y., male, aged 54 years, had recurrent attacks of pneumonia in the right lower chest for about a year. There was mucopurulent expectoration. Bronchoscopy revealed a tumor in the right lower lobe obstructing the bronchus. X-ray film showed no aeration in this lobe. The patient was running a low-grade fever. A total pneumonectomy was done without drainage on March 24, 1941, in spite of mediastinal metastasis. The lymph nodes were also removed. Section of the lung showed a tumor about 5 centimeters in diameter. It was spinocellular carcinoma of grade II malignancy. There were large bronchiectatic cavities filled with pus behind the obstruction. The resection of the mediastinal lymph nodes required a visceral pleural patch to close the mediastinal pleura. A thoracotomy was done on April 2, 1941 because of infection. A thoracoplasty was performed on May 7, 1941. The wound is now closed and the patient is apparently well.

CASE 15. R. J., male, aged 40 years, in whom at a routine insurance examination a lesion was found by x-ray film in the left lung in March, 1941. Since the lesion continued to increase in size for the next 6 months, he was referred to us. Bronchoscopy was negative. The patient had absolutely no symptoms, but the x-ray film showed the characteristic picture of a bronchogenic carcinoma. A total pneumonectomy was done without drainage on September 24, 1941. The tumor was an adenocarcinoma. The patient returned to work in his office 6 weeks after operation and has been well since.

CASE 16. W. M., male, aged 50 years, had a cough for 2 months with a recent bit of blood-streaked sputum. X-ray film showed a small area of atelectasis in the left upper lobe. Bronchoscopy revealed spinocellular carcinoma of grade II malignancy. The patient had had no other symptoms and was in his normal physical condition. A total pneumonectomy without drainage was done on October 1, 1941. The carcinoma was found to be only about 4 millimeters in diameter in the upper lobe bronchus. The patient has been perfectly well since operation was performed.

CASE 17. H. C., male, aged 62 years, had a 2 year history of suppurative disease in the left lower lobe. Bronchoscopy revealed a stricture of the left lower lobe bronchus with a pure culture of Friedlaender's bacillus. The fifth biopsy revealed spinocellular carcinoma of grade II malignancy. A total pneumonectomy without drainage was done on November 12, 1941. The patient was discharged apparently well after 3 weeks. A low grade fever developed after about a month. Sulfadiazine therapy kept the infection so well under control that drainage was not done until February 2, 1942. A thoracoplasty is yet to be done.

CASE 18. R. S., male, aged 63 years, had had a cough for 1 year, bloody sputum and fever for about 6 weeks, and about a 25 pound weight loss in the last 6 months. Diagnosis of carcinoma, squamous cell type, in the right lower lobe was made by x-ray film and bronchoscopy. Right pneumonectomy with drainage was done on February 4, 1942. Metastatic carcinoma was found in mediastinal lymph nodes. Convalescence was uneventful. Thoracoplasty is yet to be done.

Fig. 8. Case 18, 2 months after operation. The chest was drained at the time of operation because of infection. The mediastinum is now fixed. The patient is ready for thoracoplasty.

CASE 19. R. C., aged 62 years, had had pain in the right upper chest and shoulder for 2 months. X-ray film showed a tumor in the apex of the lung; bronchoscopy was negative. Exploration on February 20, 1942 revealed an adenocarcinoma adherent to parietal pleura. A total pneumonectomy was possible by removing the parietal pleura over the apex of the chest. Enlarged lymph nodes in mediastinum proved to be inflammatory. The chest was drained due to contamination of wound in removing the adherent tumor. The patient has now been free from pain and well for 2 months. A thoracoplasty is yet to be done.

CASE 20. O. J., male, aged 64 years, had had bloody sputum for 1 year, pain in the right lower chest for 6 weeks, and a 25 pound loss of weight. X-ray examination showed a tumor in the right lower lobe. Bronchoscopy revealed a squamous cell type of bronchogenic carcinoma. A right pneumonectomy was done on February 23, 1942. No metastasis was found in the mediastinum, but the tumor was freed with difficulty from the diaphragm. No drainage. The convalescence was uneventful. When seen 2 months after operation the patient had gained 15 pounds in weight and appeared well.

SUMMARY

1. The only hope of cure for the patient with bronchogenic carcinoma is surgical removal of the tumor, which usually means total pneumonectomy.

2. Total pneumonectomy offers a complete cure for the patient with extensive but unilateral suppurative disease of the lung.

3. The preoperative and postoperative care and certain points in operative technique have been discussed.

4. The mortality in the young patient should be low whether the operation is for carcinoma or for suppurative disease.

5. The mortality will probably remain fairly high in the elderly patient with carcinoma associated with other complicating diseases.

6. Twenty patients are reported upon whom total pneumonectomy has been performed with only 1 death, a mortality of 5.0 per cent.

REFERENCES

1. CRAFOORD, C. On the Technique of Pneumonectomy in Man Surgical Clinic II of the Sabbatsberg Hospital. Stockholm: Tryckeri Aktiebolaget Thwle, 1938.
2. FLICK, J. Personal communication.
3. GRAHAM, E. A., and SINGER, J. J. J. Am. M. Ass., 1933, 101: 1371.
4. HAIGHT, C. Surg. Gyn. Obst., 1934, 58: 768.
5. LONGACRE, J. J., and JOHANSMANN, R. J. Thorac. Surg., 1940, 10: 131.
6. OVERHOLT, R. H. J. Thorac. Surg., 1939–1940, 9: 17–61.
7. RIENHOFF, W. F. Bull. Johns Hopkins Hosp., 1937, 60: 372.
8. RIENHOFF, W. F. Bull. Johns Hopkins Hosp., 1933, 53: 390.

CHRONIC ARTHRITIS

H. KELIKIAN, M.D., F.A.C.S., Chicago, Illinois

ARTHRITIS is a vague term. Denoting inflammation as its basic feature, it has come to include a multitude of other lesions. Joint changes in response to allergy, to altered nerve impulse, to metabolic and mechanical imbalance and the aftermath of necrosis and collapse of the articular ends of bones have all been lumped under one name, as years ago the affections of the stomach were made hazy and confused with the now restricted, almost obsolete term, gastritis.

NOMENCLATURE

One hopes that with newer advances the diseases of the joint will be sifted and consigned each to its proper niche in a scientifically valid scheme of classification. At the present state of our knowledge, any attempt along these lines would be presumptuous; we do not know the cause of many joint lesions and there are a few whose nature is but vaguely understood. Moreover, a classification which would correlate etiological factors with corresponding pathological changes is as yet unthinkable. Excluding such well defined entities as tuberculous arthritis, neurogenic arthropathies, gout, and a few others, all one can say of the nebulous mass of chronic joint disturbances is that they are either inflammatory in nature or are the result of wear and tear, of mechanical break-down. To be sure, an inflammatory process involving a joint may eventually create mechanical incongruities, and a worn-out joint surface may in time become the nidus of self-inflicted irritation and set up an inflammatory focus. In other words, inflammatory and degenerative joint lesions may converge into one another, or even coexist.

The inflammatory subgroup of chronic arthritis has been qualified as atrophic, proliferative, rheumatoid, infectious, progressive, multiple, adhesive, ankylosing, or synovial; when occurring in childhood it is referred to as Still's disease. The other variety of chronic arthritis has also acquired an array of adjectives: hypertrophic, degenerative, traumatic, senile, menopausal, and chondro-osseous; it is also called osteoarthritis, arthrosis, Type II, arthritis deformans ulcerosa, and Heberdene's nodes. No nomenclature has yet been fully agreed upon. The English classification designating the two groups as rheumatoid and osteoarthritic makes no commitments as to the as yet unknown cause of chronic arthritis and, although it is neither adequate nor descriptive, it is the least confusing. From a pathological standpoint the adjectives *inflammatory* and *degenerative* perhaps come closest to suggesting the primary changes that occur in the two subgroups of chronic nonspecific arthritis.

From the Department of Bone and Joint Surgery, Northwestern University Medical School; Wesley Memorial and Cook County Hospitals; Chicago.

THE BIOLOGICAL BASIS OF SUBDIVISION

The salient features of the two types can perhaps be brought out by evoking certain basic facts. A joint is a connective tissue organ. It connects and supports parts and passively permits motion between them. In its typical form, a movable, or diarthritic joint consists of a cavity lined by synovial membrane and hyaline cartilage which are respectively supported by fibrous capsule and the articular ends of bones. In their evolution from mesoderm these elements follow two patterns: one biological, the other morphological. Some connective tissue remains relatively undifferentiated, hence highly reactive, in the external stratum of the synovial membrane and in the marrow spaces of the articular ends of bones. Specialized, senescent, connective tissue evolves as articular cartilage, trabeculae of bone, the surface layer of the synovial membrane, the ligaments, and the fibrocartilages. Structurally the components of the joint are assembled on sound mechanical lines so as to insure a given articulation maximum fulfilment of its function as a unit of support or of passive motion. Inflammation primarily affects the reactive elements of the joint—the external stratum of the synovial membrane and the marrow contained in subchondral cancellous spaces; the specialized connective tissues—articular cartilage and trabeculae of bone in particular—are passively displaced by adjacent inflammatory granulations, break down when their elasticity is overcome, or degenerate and die when their source of nourishment is cut off. In one instance, the pathological trend is at the start reaction on part of biologically young tissues; in the other, the early change is characterized by regression, or wearing out, of mature, specialized connective tissue elements of joint (Figs. 1, 2).

Fig. 1.

Fig. 2.

Figs. 1 and 2. The pattern of evolution of a representative joint.

Fig. 1. Embryonic knee. Photomicrograph of the sagittal section of a human embryo estimated of 10 weeks intrauterine life. There is definite morphological change with the anlage of future bones already shaped. The slits surrounding the articular ends of femur fuse to form the joint cavity. Not as definitely discernible is the biological differentiation. In certain areas as in the bone marrow, the mesodermal tissue remains relatively undifferentiated, hence highly reactive; in others, it evolves as specialized connective tissue, the articular cartilage, for example. It is proposed that rheumatoid arthritis primarily involves the former and osteoarthritis the latter elements.

Fig. 2. Adult knee. Frontal view of a surgically opened knee of a young girl. Note the smooth, glistening articular surfaces. The synovial membrane sends a slip over the margin of the articular cartilage leaving its greater central position uncovered. By virtue of its investment the marginal cartilage can react and reproduce itself; the central portion has little or no power of reactive regeneration.

RHEUMATOID ARTHRITIS

The basic feature of rheumatoid arthritis is an inflammatory reaction on the part of the comparatively undifferentiated connective tissues, and granulations thus formed erode and displace specialized elements. The relative vascularity of the external stratum of the synovial membrane and bone marrow favors here the localization of circulating irritants, and in response to the offending agent there ensues hyperemia, edema, cellular infiltration, exudate, and tissue proliferation. The synovial membrane becomes soggy, thickens (synovitis); from its loose areolar spaces, tissue fluids seep into the joint cavity (hydrarthrosis); when cells pass into the articular cavity or are shed off there results joint exudate. Later, finger-like processes of proliferated tissue project into the joint cavity (chronic villous synovitis), or they may even break loose and float in the joint fluid (rice bodies, melon seeds). Granulations formed in the external layer of the synovial membrane may extend into the surrounding structures and cause them to contract (fibrositis, periarthritic adhesions, contractures) or, what is perhaps more common, they may break through the barrier of the internal layer of the synovial membrane, creep over the articular cartilage (pannus), erode, and destroy it. Usually proliferative activity is going on in the marrow at the same time and the trabeculae of bone are thinned, displaced (atrophy). The cartilage is attacked from below as well and when the opposing cartilages are completely eaten away, the granulations contact to form adhesions (fibrous ankylosis); ultimately these connecting strands may ossify and efface the joint completely (bony ankylosis) (Figs. 3 to 10).

Rheumatoid arthritis does not in all instances run through the entire gamut of joint inflammation. The disease may proceed up to one or another phase and then arrest itself. If a mechanical incongruity has already been created—such as eroded articular surfaces, redundant capsule due to overdistention, contractures, subluxations—the joint may in time break down architecturally

Fig. 3.

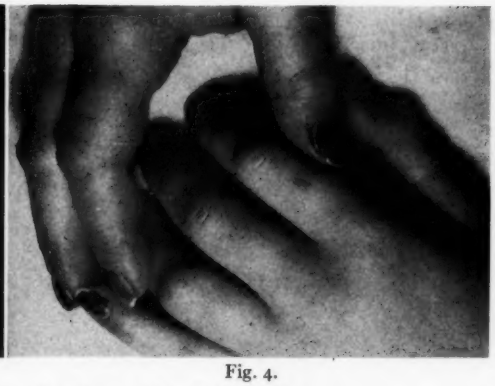


Fig. 4.

Figs. 3 to 6. Rheumatoid arthritis, active phases of joint inflammation.

Fig. 3. Hyperemia. Arthrograph of the knee of a patient with fulminant rheumatoid arthritis. A few cubic centimeters iodized oil was introduced into the knee and the films were taken every twenty minutes. Already in the first plate opaque material was seen impregnating a large popliteal node and the lymphatics leading to and away from it. Increased vascularity enhances absorption from the joint cavity.

Fig. 4. Edema. Photograph of the hands showing generalized and localized swelling in and around the proximal interphalangeal and metacarpophalangeal joints.

and evolve into the other form of chronic arthritis. Joints which are rich in biologically young, vascular, and reactive tissues—joints with extensive synovial membrane and bulbous articular ends which contain a greater amount of marrow tissue —are more likely to be affected by rheumatoid arthritis. Thus rheumatoid arthritis predilects the knees, the elbows, the metacarpophalangeal and proximal interphalangeal joints. It has been suggested that circulating irritants—bacteria, toxins, allergin, etc.,—originating elsewhere in the body as in a distant focus of infection, may give rise to rheumatoid arthritis. However, this causal relationship has not been established beyond the

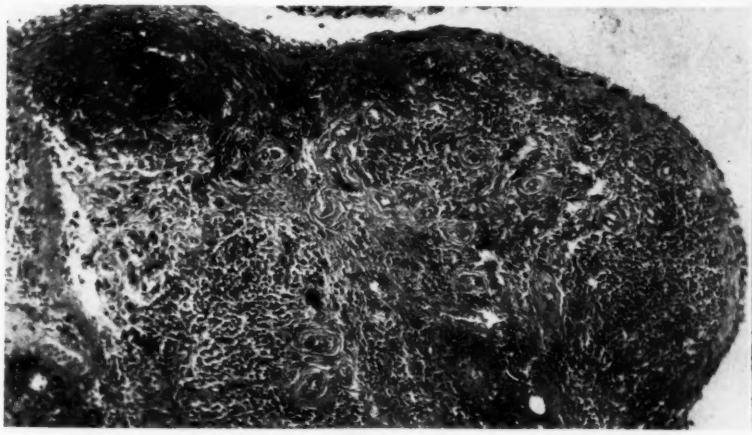


Fig. 5.

Fig. 6.

Fig. 5. Cellular infiltration. Photomicrograph through a section of the synovial membrane. Note the extensive agglomeration of cells beneath the synovial surface and the bulging of the thickened membrane into the articular cavity.

Fig. 6. Tissue proliferation. Photograph of a segment of surgically removed synovial membrane, studded with villi. The latter are finger-like processes of thickened tissue on the external stratum of the synovial membrane that invaginate internal zone and protrude into articular cavity.

Fig. 7.

Fig. 8.

Fig. 9.

Fig. 10.

Figs. 7 to 10. Rheumatoid arthritis, destructive and reparative trends.

Fig. 7. Pannus. Photograph of a surgically opened knee showing the extension of the synovial membrane over the articular cartilage of the femoral condyles.

Fig. 8. Erosion of articular surface. In this photograph of the knee the articular cartilage is further encroached upon and eaten away. Marginal granulations are continuous with those sprouting from the synovial investment of the cruciate ligaments.

Fig. 9. Ankylosis. Photograph of another surgically opened knee. Granulations have contacted and organized into scars. The jaws of the retractor are hooked to a tough band of adhesions binding the eroded articular surface of femur to the corresponding surface of tibia. This type of joint would eventually evolve into bony ankylosis.

Fig. 10. Creation of mechanical incongruity. Photograph of a surgically opened knee of a woman with long standing rheumatoid arthritis. Granulations emanating from marginal synovial membrane and from the investment of the cruciates have dug deep grooves across the femoral condyles and at their periphery. Clinically this joint was interlocked and x-ray revealed it to have merged into osteoarthritic phase. Note the overhanging and protruding spurs.

fact that a certain number of arthritics seem to benefit from eradication of foci of infection. Moreover, since some of these patients also suffer from myocardial disease, from diminished capillary circulation, and develop subcutaneous edema and nodules, it is also inferred that rheumatoid arthritis is perhaps a systemic disease involving not only joints but other derivatives of mesoderm as well (6).

OSTEOARTHRITIS

Osteoarthritis occurs most commonly in joints that bear the brunt of daily wear and tear, such as the right shoulder in a right-handed person; it affects weight-bearing joints, as the hip, knees and ankles; and, third, it predilects joints poor in blood supply, as the distal interphalangeal joint of the hands. Trauma, acute or chronic, is perhaps the main causative factor in osteoarthritis. Instances of acute trauma are found in neglected meniscal injuries, in capsular or ligamentous tears, in subluxations, and in intra-articular fractures. Chronic trauma may accrue either within the joint as a result of loose bodies, or may affect the joint indirectly by taxing the lines of stress and strain to which a given area of the articular cartilage is accustomed. Examples of such indirect force causing osteoarthritis are to be found in the weight-bearing joints of the obese and in joints near mechanical misalignments: flat feet, knock

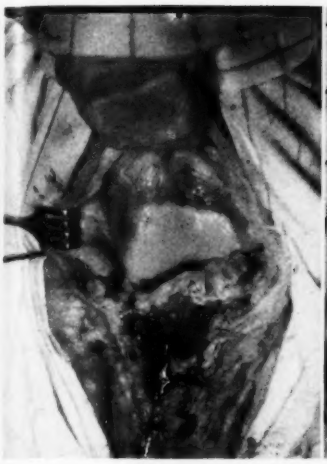


Fig. 11.

Fig. 12.

Fig. 13.

Figs. 11 to 13. Osteoarthritis, causes of degeneration of the articular cartilage.

Figs. 11 and 12. Chronic trauma due to misalignment of articular ends and unwonted friction.

Fig. 11. Photograph at the time of arthrotomy of the knee of a man who, 18 months previously, had received a depressed fracture of the upper articular end of tibia with tilting of the plateau and throwing of a bony promontory up against the medial condyle of the femur. Note the slant of the weight-bearing surface from side to side and the promontory of bone jutting up and impinging against the articular surface of the medial condyle of the femur.

Fig. 12. The same after the bony promontory had been chiseled off. Note the two circumscribed areas on the articular surface of the medial condyle of the femur. The cartilage here was soft, pitted and had lost its luster, macerated, as it were, by the abutting bone.

Fig. 13. Chronic trauma: excessive pressure. Photograph of the jack-knifed knee, obtained at autopsy, of a man whose weight in life exceeded three hundred pounds. Note the worn-out ragged areas at points of greatest pressure over the articular surface of the femoral condyles. The corresponding surfaces of tibial plateau, protected as they are by the semilunar cartilages, are comparatively unaffected.

knees, coxa vera, malunited fractures, and partially arrested epiphyseal growths. Other instances of chronic trauma are also seen in hallux valgus or supraspinatus tendon degeneration where the articular cartilage is forced to rub against rough, frayed, fibrous, or calcareous surface instead of a smooth one. Apart from trauma, age (prolonged trauma), arteriosclerosis, necrosis and collapse of the articular ends of bone, and previous inflammation or infection are also regarded as contributing factors to osteoarthritis (Figs. 11 to 13).

In osteoarthritis, the mechanical, the specialized elements of the joint are affected primarily.

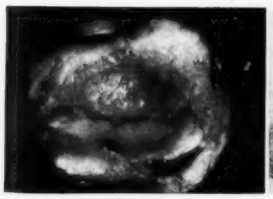


Fig. 14.

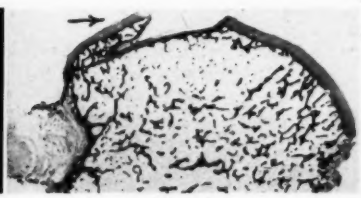


Fig. 15.

Fig. 16.

Figs. 14 to 16. Osteoarthritis, changes accompanying mechanical breakdown of the joint.

Fig. 14. Ulceration of the articular cartilage. Photograph of the proximal articular surface of the first phalanx of the great toe of a woman in late fifties, who, for years, had been wearing short shoes and high heels. The cartilage is missing in the upper half where greatest pressure was borne on account of the retracted toe; the denuded bone was worn smooth.

Fig. 15. Epiarticular ecchondrosis. Photograph of the sagittal section through the distal articular end of the metatarsal bone. The chondro-osteophyte overhangs the eroded articular surface and is piled over old bone and the remnant of old articular cartilage.

Fig. 16. Marginal ecchondrosis. Photograph of the sagittal section of another metatarsal head showing chondro-osteophytes which are protruding out from the articular surface.

Fig. 17.

Fig. 18.

Fig. 19.

Fig. 20.

Fig. 21.

Fig. 22.

Figs. 17 to 33. Surgical measures resorted to in treating rheumatoid arthritis.

Figs. 17 to 21. Skeletal traction to prevent contracture and pressure upon undermined articular surface.

Fig. 17. Photograph of a hand in banjo splint and elastic traction attached to a wire passing through the distal phalanx of the middle finger of the left hand.

Fig. 18. X-ray picture of the finger with traction wire *in situ*. The arrow points to the proximal interphalangeal joint. The distal articular end of the proximal phalanx reveals an area of erosion of the articular surface, probably produced by subchondral or marrow granulations. Motion was encouraged against elastic traction which was maintained for 2 months.

Fig. 19. The same, 3 months later with traction wire removed. Note that the distal articular cortex of the proximal phalanx, previously seen eroded, had been in part replaced.

Fig. 20. Photograph of the hand after the banjo splint had been removed.

Fig. 21. The same with hand closed showing the occlusion of the middle finger.

Fig. 22. Capsulotomy is a standard measure for overcoming flexion contracture, especially of the knee. It is at times supplemented with tenotomy and transposition of important nerves. Photograph of the lateral aspect of the knee at the time of posterior capsulotomy and section of biceps femoris tendon. Peroneal nerve is isolated and drawn away with a tape. Note the taut tendon of biceps just above it. The blade of the scalpel is inserted into the popliteal space; hugging the posterior aspect of the femoral condyles it is carried into the knee joint. The biceps tendon is subsequently released and the peroneal nerve is displaced forward to avoid overstretching while the knee is carried into extension.

The highly differentiated, hence less reactive, derivatives of the connective tissue—bone and cartilage in particular—bear the brunt of shearing and pressure stresses and break down when their elasticity is overcome, or when their nourishment is interfered with as by diminished blood supply which affects the bones, or by scant synovial fluid from which the articular cartilage partly derives its nourishment. At points of greatest friction or pressure the cartilage wears down; it loses its surface gloss, its resilience, softens and shreds (chondromalacia); the layer of cartilage nearest the joint cavity slowly disappears and the main body of the deeper cartilage splits perpendicularly to the surface (degeneration); the zone of calcification underneath cracks; the articular cortex of the bone is laid bare (arthritis ulcerosa), and denuded bone wears smooth by usage (eburnation). Secondarily, reactive changes take place in the marginal cartilage, in the synovial membrane and in the cancellous spaces of the articular ends of bones. In adults, the central pressure-bearing area of the articular cartilage is devoid of perichondrium which elsewhere in the body, as in the ribs, has the power of reproducing cartilage; the marginal portion receives a slip from the synovial membrane and can repair itself. In response to unwonted stress put upon it by incongruous articular surfaces, the marginal cartilage thickens (hypertrophy), swollen areas may bulge out on

Fig. 23.

Fig. 24.

Figs. 23 to 31. Synovectomy is another standard surgical procedure and is especially beneficial in persistant hydrops and in chronic villous synovitis.

Figs. 23 and 24. Synovectomy; the operation.

Fig. 23. Photograph of the surgically opened right knee of a man with rheumatoid arthritis who, 9 years previously, had a synovectomy performed on his left knee with a fair restoration of function and no recurrence of effusion. Note that the synovial membrane is thrown into numerous folds and villi and its secreting surface is thus greatly expanded. Also observe that the inflamed membrane has grown across the articular cartilage and partly eroded it.

Fig. 24. Photograph of the knee immediately after dissection of turgid thickened synovial membrane.

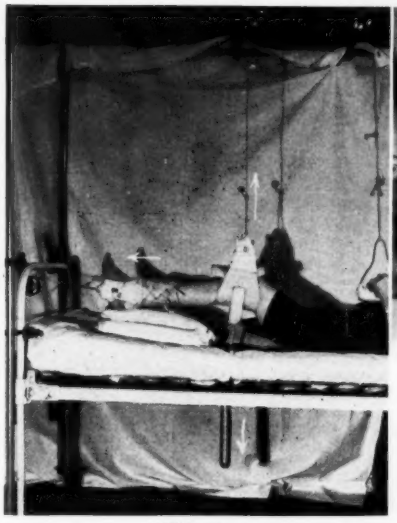


Fig. 25.

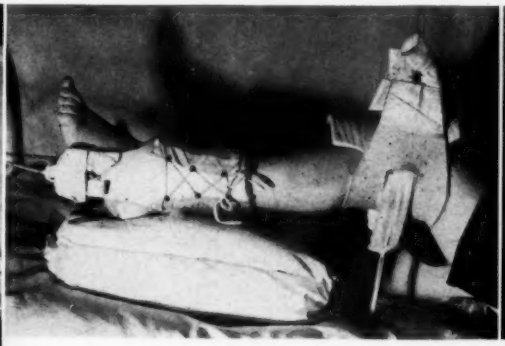


Fig. 26.

Fig. 28.

Fig. 27.

Figs. 25 to 28. Synovectomy, postoperative mobilization of the joint. This is started 3 days to 2 weeks after synovectomy, depending upon the degree of pain and the patient's willingness to co-operate.

Fig. 25. Photograph of an improvised three way traction outfit. A 5 to 10 pound weight is applied to an anklet made of felt or canvas. The patient forces the knee into flexion by means of a rope going over pulleys to a sling under the knee. As the perpendicular pull is released another 5 pound weight attached to a rope passing through a hole in the mattress forces the knee into hyperextension.

Fig. 26. Close up photograph of the three way traction outfit.

Fig. 27. Photograph of the anklet made of canvas instead of the original felt.

Fig. 28. Photograph of the two way knee sling.

Fig. 29.

Fig. 30.

Fig. 31.

Fig. 32.

Fig. 33.

Figs. 29 to 31. Synovectomy, functional results.

Fig. 29. Knees of a woman who underwent bilateral synovectomy: the left knee 3 years ago; the right a year ago.

Fig. 30. Photograph showing the degree of flexion obtained a year after operation of the right knee.

Fig. 31. Photograph demonstrating the degree of flexion attained 3 years after synovectomy of the left knee.

Figs. 32 and 33. Erasion of incongruities. This operation is not recommended in weight-bearing joints. However, if both hips and knees are interlocked or ankylosed it becomes expedient to mobilize one knee and opposite hip.

Fig. 32. Surgically opened knee shown in Figure 10.

Fig. 33. Same immediately after smoothing out crater-like mechanical incongruity, chiseling off osteophytes, and marginal synovectomy. Patella was reduced in size and reshaped. Some operators remove it completely.

Figs. 34 to 40. Surgical measures in osteoarthritis.

Figs. 34 to 37. Osteotomy is often performed to correct flexion deformities in rheumatoid arthritis. In osteoarthritis it is resorted to with the idea of shifting weight-bearing points and putting a relatively unworn, mechanically sound articular surface under the lines of stress and strain.

Fig. 34. X-ray picture of the left hip of a woman with inadequate acetabulum and osteoarthritis. The right hip was similarly affected.

Fig. 35. The same immediately after osteotomy. Two pins were introduced, one into the femoral head, the other just beneath the greater trochanter. Intertrochanteric osteotomy was performed. The pins were used to maneuver the fragments into desired position and were made to cross one another outside of the body and were incorporated in a short spica cast. Note that the femoral head has been

Fig. 34.

Fig. 35.

Fig. 36.

levered deep into the acetabulum and is somewhat rotated anteriorly. The lower fragment is displaced medially.

Fig. 36. The same 2 months later. Union has already taken place and the head of the femur is deep in acetabulum.

Fig. 37. Composite photograph of the patient a year later showing the stability of the left hip and its range of motion. This hip had ceased to hurt patient; the right hip, as yet untouched for purposes of control, continued to cause pain.

Figs. 38 to 40. Arthrodesis.

Fig. 38. Photograph of the bowed left knee of a man of 58 who some 30 years ago injured this knee which became markedly swollen. The swelling recurred for years after and at the time of examination the capsule of the joint was so lax that the knee wabbled from side to side as in a Charcot joint. Motion, however, was painful and there was no anteroposterior instability indicating intact cruciates.

Fig. 39. Photograph of the knee at arthrotomy. Note the deep ulcer over the articular surface of the medial femoral condyle where most of the weight was borne.

Fig. 40. Photograph showing the stability of the knee 6 months after fusion.

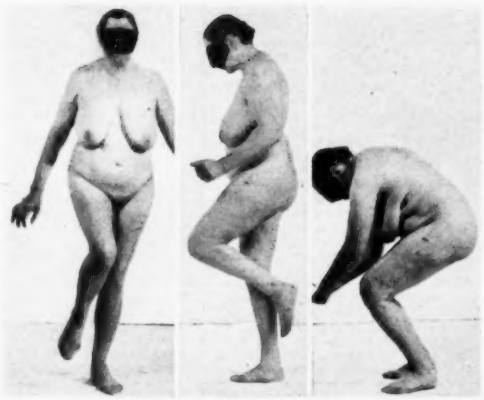


Fig. 37.

Fig. 38.

Fig. 39.

Fig. 40.

COMPARISON OF RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

	Rheumatoid arthritis	Osteoarthritis
Synonymous adjective	Atrophic, proliferative, infectious, inflammatory, etc.	Hypertrophic, degenerative, traumatic, senile, etc.
Etiological relations	Under 40 years; pale asthetic women; foci of infection	Over 40 years; robust laborers; acute or chronic trauma
Systemic reactions	Fever; leucocytosis; increased sedimentation rate may be present	Absent
Joints predilected	Those rich in primitive connective tissues—joints with extensive synovial membrane and bulbous articular ends, like the proximal interphalangeals	Weight-bearing, traumatized joints and those poor in circulation, like the distal interphalangeals
Symptoms	Pain and stiffness marked; many joints involved.	Pain and stiffness relatively mild; one, or at most, a few joints affected
Pathology	A) Primary: Inflammation of relatively primitive vascular connective tissues of the joint—of synovial membrane and bone marrow. B) Secondary: Displacement or atrophy of specialized elements of the joint—of cartilage and bony trabeculae	A) Primary: Wearing down of specialized elements of the joint—of cartilage and underlying bone. B) Secondary: Reactive process at the margins in the form of spurs.
X-ray	Fusiform enlargement of soft part; disappearance of cartilage space along the margins; osteoporosis, subluxations, contractures, and ankylosis	Broadening of articular surfaces of bones; disappearance of the space in central areas and sclerosis of bone below; spurs, "cystic areas," loose bodies
Rational of treatment	Regard the condition as a systemic disease and treat the patient as a whole, resorting to measures that would improve his health; prevent deformities	Direct attention to the joint itself; undertake measures to save it from wearing down; better its mechanics and the mechanics of the body
Surgery	Aim at putting a painful joint at rest (splintage), overcoming contractures (traction, turnbuckle splint, manipulation, capsulotomy, osteotomy, ostectomy, etc.); eradication of residual inflammation (synovectomy); mobilization of an already ankylosed joint (arthroplasty); and elimination of very painful one (arthrodesis)	Indicated in presence of painful loose bodies (arthrotomy); when there are incongruities of surfaces that might beneficially be eliminated (erasion, arthroplasty); when there are chances of proffering a better weight-bearing surface (corrective osteotomy); when the joint has crumbled down and is painful (arthrodesis)

the surface (epiarticular ecchondrosis), or they may project peripherally (marginal ecchondrosis). Surface swellings further enhance the existing incongruity and marginal growths widen the bearing area of the joint. These nodules may become vascularized and receive a bony core (chondrosteophyte); they may be completely ossified (osteophytes); they may detach and break free in the joint cavity (osteocartilaginous loose bodies). Marginal spurs encroach upon the synovial membrane and irritate it toward inflammatory reactivity, and analogous proliferation is set up in the cancellous spaces of the bone which replace the trabeculae and create cavities containing fibrous tissue or fatty marrow (cystic degeneration). The opposed articular surfaces may interlock in osteoarthritis, but true ankylosis does not occur, as nodular thickenings of the marginal cartilage prevent the central ulcerated areas from contacting (Figs. 14 to 16).

CLINICAL DIFFERENTIATION OF THE TYPES

Rheumatoid arthritis is more generalized and affects many joints; osteoarthritis is more or less confined. The symptoms of pain and stiffness are far more severe in rheumatoid arthritis and one may find the joint manifestation associated with myocardial heart disease, subcutaneous nodules, vasoconstriction, psoriasis, anemia, etc.; osteoarthritis may accompany menopause, obesity, arteriosclerosis, congestive heart disease, chronic bronchitis and bronchiectasis, and, lastly, mechanical misalignments of the body. X-ray films of the joints in rheumatoid arthritis may in the earlier stages reveal fusiform swelling of the soft parts, somewhat later disappearance of the joint space, and erosion of marginal articular cortex and porotic bone; in late stages one may see evidence of contractural deformities, of subluxations and ankylosis. Films in osteoarthritis would reveal disappearance of the joint space at pressure points, sclerosis of the bone below, cyst-like formations in the articular ends, marginal spurs, and osteocartilaginous loose bodies in the joint.

THE TREATMENT OF RHEUMATOID ARTHRITIS

In treating arthritics it is safe to regard the rheumatoid variety as a generalized, systemic disease and treat the patient as a whole. In fulminant stages, it is well to prescribe a complete physical rest, splinting the joints in optimum position of function should ankylosis intercede. The latter could at times be obviated by making the splints removable so as to permit periods of guarded exercise, or better still, one may resort to traction and countertraction instead of fixed splintage. All measures which may contribute to the general well being of the patient should be undertaken: high caloric, high vitamin diet, tonics, cathartics, analgesics, sedatives, spas, etc. Foci of infection are eliminated to give the patient the benefit of the doubt, and recourse may be taken to gold injections and vaccines as there is at least a relatively rational basis for resorting to parenteral therapy in a generalized disease like rheumatoid arthritis, which might be caused or aggravated by infections and which is hopeless at times. Thus during the earlier stages of rheuma-

toid arthritis measures resorted to are mainly medical and systemic. The surgeon veers his attention toward the local manifestations of the disease as aspirating overdistended joints, splinting painful ones and applying various forms of traction and countertraction to prevent deformities.

Apart from exercise, traction, and splintage, numerous local measures are undertaken in rheumatoid arthritis. Joint lavage with physiological salt solution is occasionally carried on to remove thick flocculent exudate from the articular cavity, and the articular ends of bones are drilled by some with the purpose of releasing pent-up granulations from the cancellous spaces (forage). Massage, heat therapy, histamine, and mecholyl iontophoresis are resorted to with the idea of improving local circulation. Massage and manipulation is not begun until the sedimentation rate has become normal and the joint inflammation has subsided. At times it becomes expedient to inflate the joint with air, oxygen, saline, or iodized oil, and then manipulate it. Injection of such material purports toward breaking or slackening adhesions. Manipulation should not be forceful; it is safer to use less force and repeat the procedure. A joint requiring great force had better be operated upon so as to sever tough adhesions surgically—either within or around the joint capsule. In smaller joints it might be wiser to enhance intra-articular adhesions in order to eliminate painful motion. This is done by injections of sclerosing solutions (quinine urea hydrocholoride) and immobilizing the joint for a long time. Capsulotomy, osteotomy, or tenotomy aim at correcting resistant deformities. The same end may also be attained by wedging the cast and correcting the deformity by a well placed turnbuckle. Deformities may likewise be corrected by skin or skeletal traction. Synovectomy is sometimes resorted to when the inflammation has left an extensive ever-secreting surface (hydrops, chronic villous synovitis). As to the comparative value of arthrodesis and arthroplasty, it can in general be stated that one must aim toward procuring a mobile joint in the upper extremity and a stable, even though stiff, one in the lower. Therefore arthroplasty, especially of an old ankylosed elbow, is at times commendable. A stiff painless knee or ankle, when in good position, had better be left alone. When both hips and knees are ankylosed one may compromise at mobilizing the hip on one side and the knee on the other, leaving a painless fused hip and knee. In rare instances the bones are shortened to release contracted tendons. Removal of one or both rows of carpal bones would accomplish the same (Figs. 17 to 33).

THE TREATMENT OF OSTEOARTHRITIS

The treatment of osteoarthritis is mainly local. Obesity when present is reduced by regulated doses of thyroid and diet; postural defects indirectly affecting the joint are corrected. Painful joints are supported by fixed or ambulatory splints. Heat, massage, and analgesics are prescribed to alleviate pain. Arthrotomy is at times performed for removing osteocartilaginous loose bodies; occasionally painful osteophytes are chiseled off, irregularities of articular surfaces smoothed (cheilotomy, débridement, reconstruction, erasion). In the hip, of late, vitallium arthroplasty has come into vogue; at times, again in mallum coxae senilis, osteotomy is performed so as to shift the weight-bearing lines and proffer an undamaged articular surface under the lines of stress and strain. Arthrodesis is performed to eliminate crumbled weight-bearing joints (Figs. 34 to 40).

SUMMARY

The accompanying table attempts to recapitulate and contrast the basic features of the two great forms of chronic nonspecific arthritis.

REFERENCES

1. Allison, Nathaniel, and Ghormley, R. K. Diagnosis of Diseases. New York: William Wood & Co., 1931.
2. Cecil, Russell L. Oxford Monographs on Diagnosis and Treatment. Vol. VI. New York: Oxford University Press, 1936.
3. Ely, Leonard W. Inflammation in Bones and Joints. P. 16. Philadelphia: J. B. Lippincott Co., 1923.
4. Fisher, A. G. Timbrell. Chronic (Non-Tuberculous) Arthritis. Pp. 7–35. London: H. K. Lewis & Co., Ltd., 1929.
5. Hench, P. S. Acute and Chronic Arthritis. Orthopedic Surgery. New York: Thomas Nelson and Son, 1938.
6. Kelikian, H. Surg. Gyn. Obst., 1940, 71: 416–436.
7. Magnuson, P. B. Surg. Obst. Gyn., 1941, 73: 1–9.
8. Nichols, and Richardson. J. Med. Res., 1909, 16: 149.
9. Osgood, R. B. J. Bone Surg., 1926, 8: 1.
10. Wilson, P. D. J. Bone Surg., 1929, 11: 40.

OSTEOCHONDROMAS ARISING FROM THE BASE OF THE SKULL

CARL FELIX LIST, M.D., Ann Arbor, Michigan

INTRACRANIAL tumors of cartilaginous structure are among the most unusual types of neoplasm encountered by the neurologic surgeon. Such lesions may arise from the meninges or from the bones of the skull. The meningeal chondroblastomas appear to be an unusual variant of the common meningioma. Approximately 30 of such cases have been hitherto reported, and a good review of the literature pertaining to them is given by Chorobski, Jarzymski, and Ferens.

The osteochondromas arising from the base of the skull exhibit a characteristic anatomical and clinical picture, the description of which is the purpose of this study. In view of the rare occurrence of the basal osteochondroma as many observations as possible were utilized. The author was fortunate enough to be able to review a composite material of 7 examples: 5 cases were seen in the University of Michigan Hospital (3 of these were personal observations) and 2 were taken from Dr. Harvey Cushing's series of intracranial tumors, having been made available to me through the kindness of Dr. Louise Eisenhardt, in charge of the Brain Tumor Registry in New Haven.

The illustrative case histories to follow will be divided into two groups: (1) primarily intracranial osteochondromas, arising from the sphenoid bone (5 cases); and (2) primarily extracranial osteochondromas of the ethmoidal or sphenoidal region with secondary intracranial extension (2 cases).[1]

REPORT OF CASES

Primarily intracranial osteochondromas arising from the sphenoid bone

CASE 1. Sanford D., No. 477,321, U. of Mich. Hosp., male, aged 32 years, was referred by Dr. F. Barbour, of Flint. Patient presented the clinical syndrome of a right-sided parasellar lesion of several years' duration. There was roentgenographic evidence of parasellar and retrosellar calcification. Osteoplastic craniotomy was performed with apparently complete removal of an extradural osteochondroma. Patient recovered but with residual neurologic signs.

For 7 years prior to admission, the patient gained weight rapidly until he reached the weight of 270 pounds. At the same time, he noted increasing thirst and polyuria. Two years before admission, vision of the right eye began to fail. This progressed gradually, and later he noted visual loss also on the left. For the 6 months prior to admission, he had suffered from paroxysmal right fronto-occipital headaches and retro-orbital pain, occasionally accompanied by vomiting, and had experienced diplopia and drowsiness. Recently he had become impotent and complained of numbness of the right half of the face.

Examination revealed the following: Patient was a very obese man, weighing 270 pounds with a florid complexion and sparse beard; otherwise there were no constitutional changes. He showed no gross mental change except for slight euphoria and indifference. There was mild right temporal and supraorbital tenderness. Visual acuity was 6/9 on the right and 6/4.5 on the left. The right optic disc showed slight temporal pallor. A partial incongruous homonymous hemianopsia to the left and bilateral paracental scotomas were present. The mydriatic right pupil did not react to light and on accommodation, but the left pupil was normal. There was a considerable paresis of the right superior rectus, and slight paresis of the inferior oblique and inferior rectus. Although the corneal reflexes were normal and equal, sensation of the right cornea was slightly diminished and cutaneous hypesthesia existed in the first trigeminal division on the right. The patient showed a minimal, left lower facial weakness and slight unsteadiness of the left arm. Deep reflexes were slightly hyperactive on the left, with a positive Hoffman reflex. The left abdominal reflexes were diminished.

Roentgenograms of the skull revealed slight erosion of the dorsum sellae. There was a dense, mottled intracranial calcification in the right parasellar, suprasellar, and retrosellar areas. It extended from the anterior clinoid to the petrous ridge, covering the floor of the right middle fossa (Fig. 1, a).

Diagnosis: Right parasellar and retrosellar tumor, presumably a calcified meningioma or osteochondroma. A craniopharyngioma was also considered as a less likely diagnostic possibility.

Operation was performed March 2, 1941, by Drs. C. F. List and M. M. Peet; local anesthesia, supplemented by intravenous sodium pentothal, was used. A right fronto-temporal osteoplastic craniotomy was performed followed by a subtemporal decompression. After the dura was opened, the brain appeared under no increased tension. Inspection of the chiasmal region showed the right optic nerve and carotid artery to be displaced forward, but no tumor was visible. An exploring needle introduced into the second temporal convolution toward the base met firm resistance at a depth of 3 centimeters. Thereupon the anterior two-thirds of the right temporal lobe were resected. A nodular tumor, the size of a large plum, was seen to arise extradurally from the base of the middle fossa and to

From the Department of Surgery, University of Michigan Medical School, Ann Arbor, Michigan, and the Brain Tumor Registry, Yale University School of Medicine, New Haven, Connecticut.

[1] Nearly 60 cases of chondroma of the ethmoid and nasal cavities are recorded in the otorhinological literature (Hickey), but only those with neurosurgical implications (intracranial extension) will be considered here.

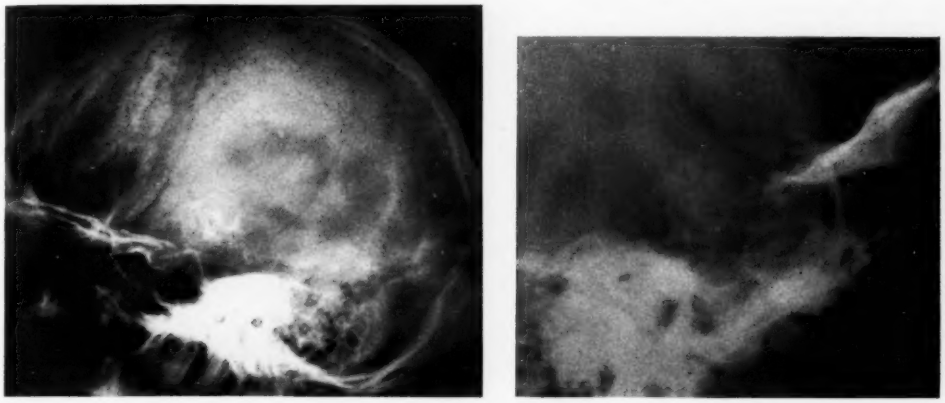


Fig. 1. Roentgenograms[1] of intracranial basilar osteochondromas. Calcified parasellar tumors in lateral projection. a, left, Case 1; b, Case 4.

occupy the entire parasellar and retrosellar area, where it had penetrated the dura (Fig. 3). The grayish white tumor was firm and gritty in parts due to calcification. It had the typical appearance of an osteochondroma. At first, the main bulk of the tumor was removed piecemeal, and then its attachment along the cavernous sinus and posterior clinoid process was exposed by splitting the basilar temporal dura. Considerable hemorrhage from the superior petrous sinus and veins surrounding the gasserian ganglion was controlled by electrocoagulation. After the dura was split over the clivus, the tumor was seen to extend both extradurally and intradurally in front of the pons, but the arachnoid (basilar pontine cistern) was intact. The right 3d, 5th, and 6th nerves were exposed. All visible tumor tissue was removed.

Histologic report: Cartilaginous tissue with large areas of degeneration, calcification, and bone formation. Diagnosis: Osteochondroma (Fig. 5, a).

Immediately after operation the patient showed total paralysis of the right 3d, 4th, 6th, and 7th nerves, and increased involvement of the 5th nerve. Furthermore, there was marked loss of vision in the right eye, moderate left hemiparesis and homonymous hemianopsia. However, on patient's discharge from the hospital, 17 days after operation, the left hemiparesis had cleared up completely.

When the patient was last seen, a year and 10 months after operation, he had no complaints except for two generalized convulsive attacks. He stated that the polyuria and polydipsia had disappeared. Examination revealed the area of decompression to be sunken in. There was still paralysis of the right 3d and 4th nerves, and paresis of the 6th and 7th nerves, but the 5th nerve had recovered completely. Vision was normal, but bilateral mild primary optic atrophy and a slight left hemianopic field defect was demonstrable. Check-up roentgenograms of the skull showed no evidence of recurrence, viz., absence of calcifications and unchanged position of the silver clips in comparison to the first postoperative films.

CASE 2. Celena M. LeB., Peter Bent Brigham Hospital, Surg., Nos. 21203 and 40491, female, aged 26 years, was referred by Dr. M. V. Tyrode, Boston. Right parasellar syndrome had been present for 3 years. There was roentgenographic evidence of right parasellar calcification. An osteoplastic craniotomy with subtotal removal of parasellar osteochondroma was done. Patient was followed-up for 17 years after operation; eventually she showed signs of recurrence of tumor with extension into the right cerebellopontine angle.

Three years prior to admission, the patient noted numbness of the right side of the face associated with swelling of the right eyelid. This gradually receded, except for residual numbness of the right half of the forehead. With the onset of numbness, the patient experienced diplopia, especially on downward gaze. A few months later, she complained of right supraorbital headaches which were occasionally associated with vomiting. Two years before admission, the right pupil became dilated and vision of the right eye slowly declined. Menstruation remained normal.

Examination revealed the following: Patient was of normal constitutional type and free from gross mental disturbances. The right temporal region was tender to percussion. Vision was 20/20 in left eye, 20/30 in right eye. There was slight right optic atrophy with mild concentric contraction of the right visual field. The dilated right pupil hardly reacted to light and on accommodation. There was incomplete paralysis of the right 3d nerve, namely paralysis of the inferior rectus, moderate paresis of the superior rectus and inferior oblique, and slight weakness of the medial rectus. The right 4th nerve was totally paralyzed, the right 6th nerve paretic. There was hypesthesia in the ophthalmic division of the right 5th nerve, with depression of the corneal reflex; mild hypesthesia was present also in the second trigeminal division. The deep reflexes of the left upper extremity were increased and the left abdominal reflexes were diminished.

Roentgenogram of the skull showed that the right anterior clinoid process was slightly eroded. There was a dense right parasellar calcification of cauliflower appearance extending from the lesser sphenoidal wing almost to the midline and outward to the middle of the right temporal fossa.

Diagnosis: Calcified right parasellar tumor, presumably a meningioma arising from the inner portion of the right sphenoidal wing. An osteochondroma was also considered.

Operation was performed on May 12, 1924, under ether anesthesia, by Dr. Harvey Cushing. A right-sided low osteoplastic flap was turned and a subtemporal decompression added. When the dura was opened, the brain was

[1]Roentgenograms were slightly retouched before reproduction.

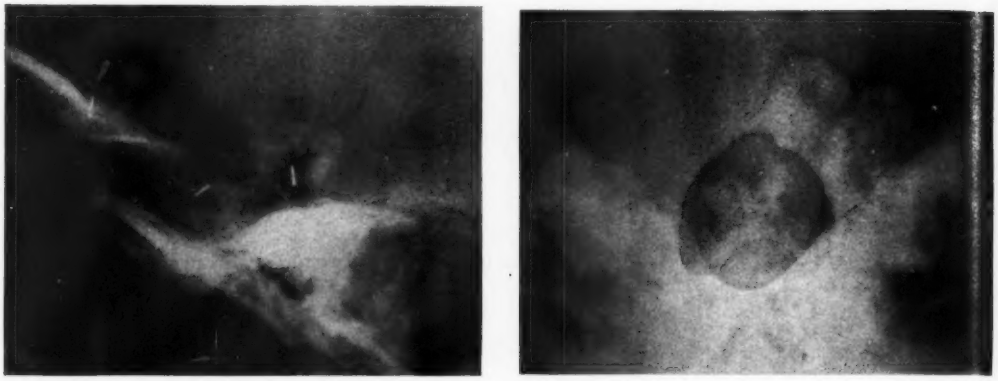


Fig. 2.[1] Calcified parasellar tumor extending into the cerebellopontine angle, Case 2. a, left, Lateral projection; b, occipital projection.

found to be of normal appearance and under no increased pressure. Elevation of the temporal lobe, however, revealed a smooth, round, extradural tumor arising from the posterior medial part of the right middle fossa. When the overlying dura was incised the tumor was found to have the appearance of a soft chondroma containing yellowish calcified areas; 25 grams of the growth, including its anterior pole, was removed piecemeal. Hemorrhage from the raw bed of the tumor was controlled by muscle packs.

Histologic report: The tumor was a calcifying myxochondroma.

After operation, there was complete right ophthalmoplegia, but the trigeminal symptoms cleared up. Check-up roentgenograms showed a few remaining calcifications in the right middle fossa. The ophthalmoplegia began to improve 3 months after operation, and re-examination 2 years later showed only a residual paralysis of the 6th nerve and rigidity of the right pupil. After 3 years of postoperative observation, however, signs of recurrence became evident: She complained of right fronto-occipital headaches and dizziness. She also suffered from attacks of general weakness associated with facial flushing and peculiar epigastric sensations, usually after breakfast. On one occasion, she apparently had an uncinate seizure.

When she finally began to complain of stiffness of the neck and unsteady gait, she was readmitted to the hospital (on February 3, 1932, almost 8 years after her first admission). At that time, marked decrease of vision of the right eye and bilateral mild secondary optic atrophy were noted. The right ophthalmoplegia and the lesion of the first and second trigeminal branches had recurred. In addition, there were slight nerve deafness and cerebellar signs on the right. Roentgenographic examination showed considerable increase of the calcified mass, especially in the retrosellar area with extension into the right cerebellopontine angle (Figs. 2a and b). Patient was discharged without operation.

She was last seen on May 7, 1941—17 years after operation and 20 years after onset of her disease. At that time the clinical picture was almost unchanged, but roentgenograms showed increase of subtentorial calcification.

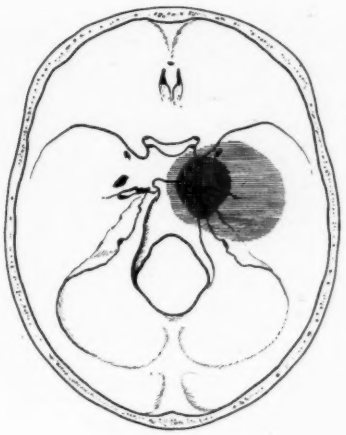
Case 3. Helen L., Peter Bent Brigham Hospital, Surg. No. 31618, female, aged 30 years, was referred by Dr. Charles Elsberg, New York, New York. Patient gave a 6-year history of right-sided calcifying parasellar chondroma. Removal of neoplasm elsewhere had been done, 2 years before admission. A second operation with excision of recurrent tumor was carried out but there was gradual spread of the lesion to the chiasmal region and cerebellopontine angle. Death occurred 13 months after second operation. No autopsy was performed.

Six years prior to admission, the patient complained of blurred vision on the right. A few months later, she began to suffer from sharp right supraorbital pain and generalized headache which were sometimes accompanied by nausea and vomiting. Four years before admission, she experienced pains in the right half of the face, followed by numbness, first of the forehead, later of the right cheek. Shortly hereafter, right ptosis and an inward squint developed. Two years before entrance, she became almost blind in the right eye. At that time (1926) Dr. Elsberg removed a chondroma of the right middle fossa by means of a subtemporal decompression. After temporary improvement of the ocular symptoms, there was evidence of recurrence, vision again failed on the right side and the right eye began to protrude. She experienced peculiar seizures, lasting for a few seconds: "An undescribable frightening sensation rushed through her body holding her lax and motionless." She also complained of occasional tinnitus and had been amenorrheic for the past year (result of x-ray therapy?).

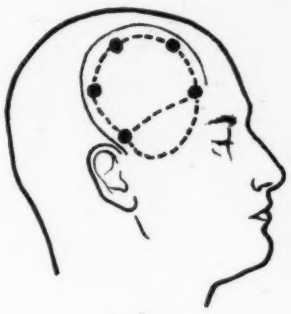
Examination revealed the following essential neurologic findings: The apprehensive, highly strung patient showed an operative scar in the right temporal region with a bone defect (decompression). Auscultation over this area disclosed a loud systolic bruit. Vision was reduced to light perception on the right, but was normal on the left. The right visual field could not be taken, the left one showed slight concentric constriction. There was right primary optic atrophy; the left optic disc was normal. The enlarged right pupil reacted only slightly to light and on accommodation. There was total paralysis of the right 6th nerve and paresis of the right 3d and 4th nerves (including a right ptosis). The first and second divisions of the right trigeminal nerve were anesthetic, the third division was hypesthetic. There was corneal areflexia and paresis of the masticatory muscles on the right.

Roentgenogram of the skull showed right parasellar erosion with scattered areas of calcification in the right parasellar and temporal regions.

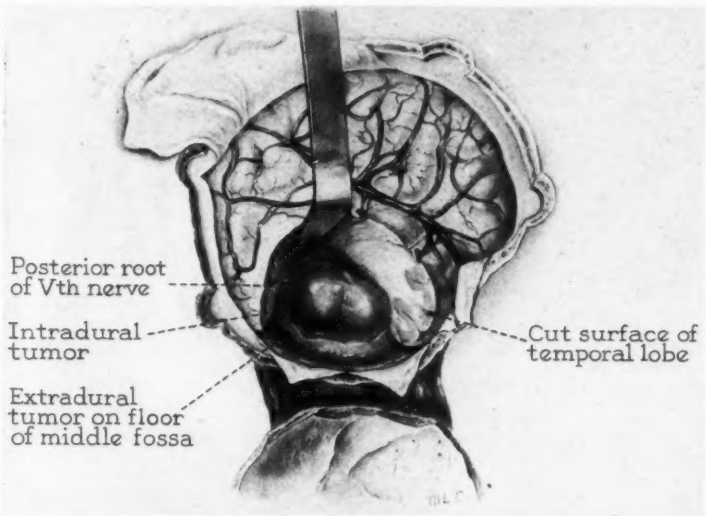
[1] Roentgenograms obtained through the kindness of Dr. M. C. Sosman, Boston, Massachusetts.



a



b



c

Fig. 3. Basilar osteochondroma, arising from the right parasellar region, Case 1. a, Diagram showing the tumor projected on the base of the skull. Attachment of tumor is cross-hatched. b, Drawing to show operative incision and osteoplastic flap. c, Tumor exposed at operation, after partial resection of the right temporal lobe.

Diagnosis: Recurrent calcifying chondroma in the right parasellar region.

Operation was performed on June 30, 1928, under local anesthesia, by Dr. H. Cushing. A right temporal osteoplastic flap was turned and the dura was opened. After incision of the second temporal convolution, a hard nodular chondroma was exposed, arising from the base of the skull. The tumor was firmly attached to the tentorium and floor of the middle fossa. It extended forward beyond the sphenoidal wing which was eroded, and posteriorly to the incisura tentorii. The neoplasm was removed by piecemeal enucleation, and weighed 28.5 grams. Considerable hemorrhage from the base, presumably from an enlarged middle meningeal artery, was controlled by implants of muscle.

Histologic reports: The fresh specimen, examined by supravital technique, showed the picture of a chondroma. This was confirmed by stained preparations which revealed irregular islands of cartilaginous cells surrounded by a collagenous or mucinous matrix. The neoplasm was considered as a nonencapsulated chondroma likely to recur.

a

b

c

Fig. 4. Roentgenograms of primarily extracranial osteochondromas, with intracranial extension. a, Osteochondroma of the sphenoid and paranasal sinuses destroying the base of the skull. Case 6. Basilar projection. b and c, Frontoethmoidal osteochondro(sarco)ma, Case 7. b, Posteroanterior projection; c, lateral projection.

The patient showed total right ophthalmoplegia after operation, but her headaches were relieved for 6 months. They then recurred and there was rapid progression of abnormal neurologic signs. When the patient was re-examined a year after operation, the subtemporal decompression was bulging. The right eye was blind and showed neuroparalytic keratitis. There were optic atrophy and temporal hemianopsia on the left. The right 3d, 4th, 5th, and 6th nerves were completely paralyzed and the 7th and 8th nerves paretic. Check-up roentgenograms showed increase of parasellar erosion with partial destruction of the right lesser sphenoidal wing and petrous apex. The calcifications also had increased and the silver clips were displaced in comparison to previous films. Evidently, the tumor had recurred and extended forward around the chiasm as well as posteriorly into the right cerebellopontine angle. One month later, the patient's death was reported. No autopsy was obtained.

The entire known duration of the disease in this patient's case was 7 years.

CASE 4. Bertha S., U. of Michigan Hospital, No. 463983, female, aged 50 years, was referred by Dr. W. D. Towsley, Midland, Michigan.

Patient suffered an acute onset of paresis of the right 3d and 4th cranial nerves without roentgenographic changes of the skull. Infraclinoid aneurysm of the internal carotid artery was suspected and the right common carotid artery was ligated. Twenty months after onset, a typical right cavernous sinus syndrome, extensive bone destruction and calcifications in the right parasellar region, had developed. Osteoplastic craniotomy was performed and a subtotal removal of an extradural osteochondromyxosarcoma was accomplished with symptomatic relief.

Since adolescence, the patient had suffered from right-sided menstrual migraine. For 2 weeks prior to her first hospital visit, on July 8, 1940, she had had severe pains in and above the right eye, occurring especially at night. Three days after onset of pain, the right upper eyelid drooped and became puffy, diplopia developed, and vision of the right eye began to fail. Examination revealed marked paresis of right 3d and 4th cranial nerves without other neurologic manifestations. Roentgenograms of the skull were normal.

The patient was seen again 6 months later, when she complained of increased pain in the right frontal and malar areas. In addition to the paresis of 3d and 4th nerves

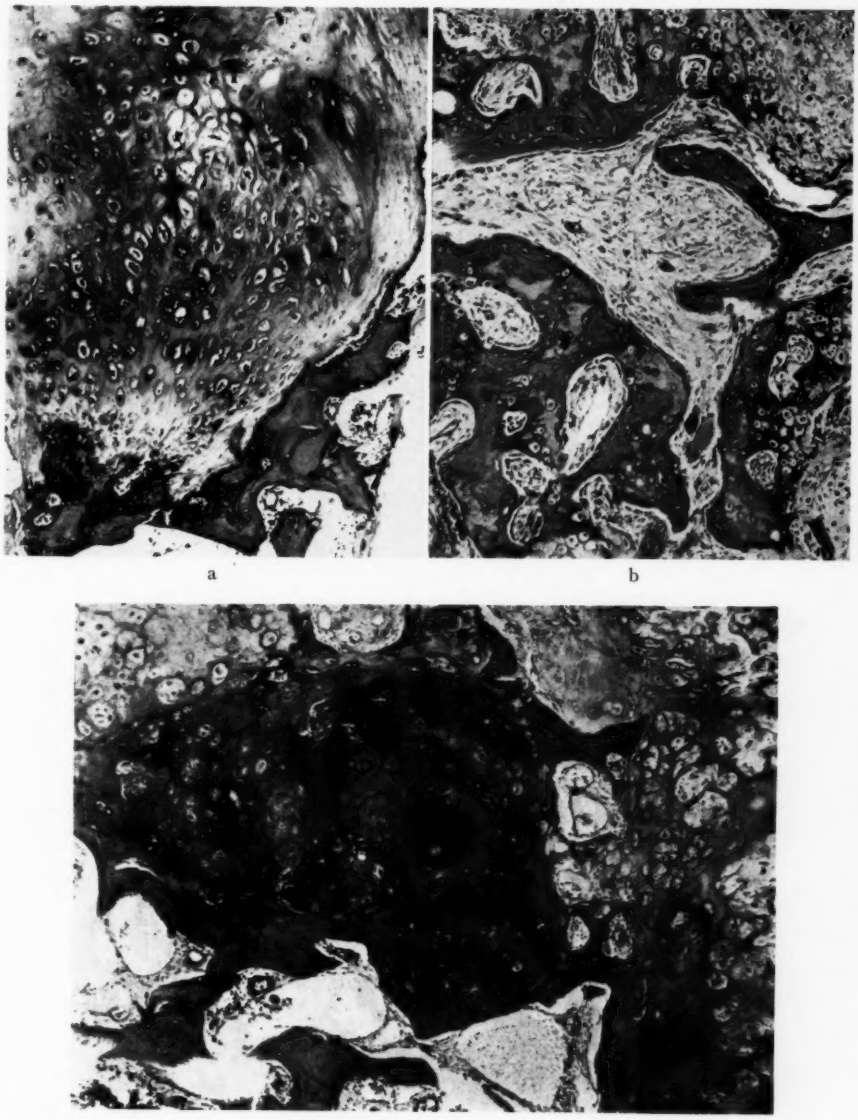


Fig. 5. Histologic sections of osteochondromas. a, Case 1, osteochondroma; b, Case 4, osteochondromyxosarcoma; c, Case 6, osteochondroma.

paralysis of the right 6th nerve and supraorbital hyperesthesia had developed. Two months later, the patient again returned because of the almost continuous and severe pain in the right frontal, orbital temporal, and malar regions. Pain often was associated with nausea, vomiting, and photophobia. Objective clinical findings were unchanged.

A tentative diagnosis of infraclinoid aneurysm of the right internal carotid artery was made. Arteriography of the right common carotid artery failed to demonstrate the internal carotid, but showed filling only of the external carotid. The roentgenograms also revealed a small flake of calcium in the right parasellar area which was then

interpreted as being in the wall of the supposed aneurysm. Ligature of the common carotid artery was performed, but afforded no relief.

The patient was not seen until a year later (March 24, 1942). She then stated that after temporary improvement, the pains in the right side of her head had become unbearable. One month prior to this last visit, numbness developed over the right side of the forehead and cheek, and vision of the right eye had become very poor.

Examination revealed the following: Patient was suffering from severe pain in the right frontal, temporal, and malar areas, and complained of nausea and photophobia. The right temporal and supraorbital regions were tender to percussion. The right upper eyelid showed ptosis and slight edema. Mild exophthalmos was noted on the right. Signs of involvement of various cranial nerves were confined to the right side as follows: Hyposmia; marked reduction of visual acuity (2/60 right eye); concentric constriction of visual field with enlarged blind spot and slight pallor of optic disc; total paralysis of the 3d, 4th, and 6th cranial nerves. The right corneal reflex was abolished and all forms of sensation were markedly diminished in the area supplied by the first trigeminal division and moderately impaired in that of the second division. There was also slight atrophy and weakness of the masticatory muscles. On the left side, the deep reflexes of the extremities were slightly increased and a positive Babinski sign was elicited.

Roentgenograms of the skull revealed extensive destruction of the sella turcica, sphenoidal sinus, basilar bone, and medial parts of the floor of the right middle fossa. There were dense calcifications in the right parasellar region extending from the inner portion of the right middle fossa slightly beyond the midline (Fig. 1, b).

Diagnosis: The previous diagnosis of carotid aneurysm was now considered untenable and a right parasellar osteochondrosarcoma was suspected.

Operation was performed on March 30, 1942, under avertin anesthesia, by Dr. C. F. List. A right-sided frontotemporal osteoplastic flap was turned and combined with a subtemporal decompression. After the dura was opened, the brain showed wide subarachnoid channels and was under no increased tension. Inspection of the chiasmal region revealed the right optic nerve to be displaced forward. After resection of the lower third of the anterior part of the temporal lobe, an extradural tumor was exposed at the medial part of the right middle fossa. The lesion was the size of a plum and felt soft, almost fluctuant. Aspiration yielded brownish gelatinous tumor tissue. Thereupon the bulging dura was incised, thus exposing the smooth avascular surface of the tumor, over which the first and second trigeminal branches were considerably stretched and elevated. These nerves were resected. The tumor was removed piecemeal and by suction. It was partly gelatinous and mucinous, partly fibrous, and partly calcareous. It extended far into the sphenoid and basilar bones and invaded the sphenoidal sinus across the midline. Total removal was obviously impossible. The large raw bed of the tumor oozed considerably, necessitating the insertion of muscle stamps.

Histologic report: The operative specimens had the structure of an osteochondromyxosarcoma of moderate cellularity (Fig. 5, b).

Except for a mild superficial wound infection which healed under sulfathiazole treatment, the patient made a good recovery and was discharged 29 days after operation. Pain, nausea, vomiting, and photophobia had ceased completely. Visual acuity improved to 6/30. There was complete anesthesia in the first and second divisions of the right trigeminal nerve and the total ophthalmoplegia persisted. Postoperative roentgenograms showed the extensive erosion of the base of the skull to a better advantage than the preoperative films. A few residual calcifications were still visible at the left side of the sphenoid body. When the patient was examined last, 8 months after operation, there was evidence of further progression of the lesion: Vision of the left eye was failing, and there was a left superior temporal quadrantic defect of the left visual field. New roentgenograms revealed recurrence and further extension of the intracranial calcification.

In the following case, the intracranial chondroma was a manifestation of generalized chondromatosis.

CASE 5. Gordon H. P., U. of Michigan Hospital, No. 155763, male, aged 21 years, was referred by Dr. Seybold, Jackson, Michigan. Multiple osteochondromas of right leg and pelvis had been present for more than 12 years. There had been present a chiasmal syndrome of 6 months' duration, with intrasellar and retrosellar calcification. Frontal osteoplastic craniotomy with partial removal of retrosellar osteochondroma was performed. Death occurred outside of the hospital, 1 month after operation. No autopsy was performed.

The patient sustained a pathological fracture of the right femur, at the age of 5 years. A painless swelling developed at the distal part of the right tibia, when he was 8 years old. One year later, pain and swelling occurred at the old fracture site. Examination then (1926) showed a bony hard swelling of the proximal portion of the right femur and a similar smaller mass at the lower end of the right tibia. Roentgenograms revealed extensive areas of bone destruction and pathological calcifications of the pelvic bones, right femur, fibular head, and tibia. Exploration of the lesion of the femur disclosed a central osteochondroma. After implantation of a bone graft, the patient recovered and was not heard of until 12 years later. Six months prior to admission, he noticed progressive failure of vision of the right eye and later a similar condition of the left eye.

Examination revealed multiple chondromas of the right leg. This leg was shortened, due to the old femoral fracture. There were also multiple cavernous hemangiomas of the oral cavity. Neurologic signs were confined to changes of the optic pathways: Visual acuity was reduced to 6/30, left eye, and 6/60, right eye. The visual fields showed bilateral central scotomas and tendency to bitemporal hemianopsia with superimposed concentric constriction. Both optic discs were abnormally pale.

Roentgenograms of the skull revealed erosion of the anterior and posterior clinoid processes without sellar enlargement. There were areas of dense calcification within the sella extending to the retrosellar and left parasellar region.

Diagnosis: An intrasellar and retrosellar craniopharyngioma was suspected. The chondromas of the right leg were considered as independent lesions.

Operation was performed on August 26, 1938, under avertin anesthesia, by Dr. M. M. Peet. A right frontal osteoplastic flap was turned and the chiasmal region was exposed. The chiasm was found to be displaced anteriorly by an encapsulated extradural tumor. After incision of the capsule, gelatinous semisolid tissue was removed piecemeal. The neoplasm seemed to originate from the posterior clinoid processes. Its total removal proved to be impossible.

Histologic report: The tumor was a myxoosteochondroma. The specimen also contained some fragments of normal anterior pituitary lobe.

Although there was no immediate improvement of vision, the patient made a seemingly uneventful recovery and was discharged from the hospital, 25 days after operation. A week later, however, the patient's mother described his condition as "extremely weak" and shortly thereafter his death was reported by the referring physician. No autopsy was obtained. It was suspected that this patient might have died from postoperative cachexia hypophysiopriva.

Primarily extracranial osteochondromas of the ethmoidal or sphenoidal regions with secondary intracranial extension

CASE 6. Claire C., U. of Michigan Hospital, No. 425277, female, aged 37 years, was referred by Dr. C. King, Toledo, Ohio. Patient presented an osteochondroma of the left maxillary antrum, floor of orbit, and ethmoid, of 17 years' duration. First evidence of intracranial involvement was 7 years after onset; definite signs of right parasellar lesion appeared a year later. Trigeminal rhizotomy was done for intractable pain. Extensive extradural and intradural spread of neoplasm noted at the base of the skull. Patient is still alive 17 years after onset, with multiple cranial nerve palsies.

In 1925, 13 years prior to admission, an osteochondroma was removed from the left maxillary antrum; the tumor had invaded the floor of the orbit and the ethmoid cells. Vision of the left eye failed shortly after operation. Six years later (1931) a recurrent tumor was removed from the ethmoid and sphenoid sinuses and deep x-ray therapy was given. A year later (1932) roentgenograms of the skull showed for the first time erosion of the right anterior clinoid process indicative of intracranial extension. In the following year (1933) roentgenograms showed destruction of the posterior wall of the right orbit (major sphenoidal wing) and right parasellar erosion and calcification. Two years later (1935), sclerotic and proliferative changes were noted in the sphenoid body and at the roof of the nasopharynx. There was also involvement of the right frontal and maxillary sinuses. In 1937, one year prior to admission, vision of the right eye declined gradually. One month before entrance, severe trigeminal pains developed, involving mainly the right second division.

Examination revealed the following: The dilated right pupil reacted hardly to light; the left pupil showed sluggish response. Vision was markedly reduced bilaterally (on the left due to vitreous opacities). The right fundus was normal, the left one could not be seen. Except for corneal areflexia on the right, there was no other trigeminal involvement.

Roentgenograms of the skull revealed extensive destruction and bony proliferation of the sphenoid body (Fig. 4, a) ethmoid cells, and all other paranasal sinuses. There were erosion and intracranial calcifications in the right parasellar region.

Diagnosis: Recurrent osteochondroma of the paranasal sinuses with involvement of the base of the skull and intracranial extension to the right parasellar area. It was decided to relieve the patient's pain by trigeminal rhizotomy.

Operation was performed on July 29, 1938, under local anesthesia, by Dr. M. M. Peet. The region of the right gasserian ganglion was exposed by the usual subtemporal extradural approach. When the trigeminal sheath was opened, the ganglion was found to be surrounded by gelatinous tumor. The basilar dura was then widely opened and the exploration carried far anteriorly and posteriorly. There was diffuse intradural as well as extradural infiltration of tumor, from the posterior to the anterior fossa, where the neoplasm was largest. Approximately 30 grams of neoplastic tissue was removed. The entire gasserian ganglion and the adjoining motor root were resected.

Histologic report: The specimen showed an osteochondroma with locally infiltrative tendency. The gasserian ganglion was surrounded, but not invaded, by tumor. (Fig. 5, c).

Following operation the patient was free from pain. There was not only total sensory and motor trigeminal paralysis, but also complete external and internal ophthalmoplegia and blindness on the right. Subsequently, the patient was repeatedly re-examined. The paralysis of the right 2d to 6th cranial nerves remained unchanged. Two years after operation, she developed right-sided otitis media and dacryocystitis. Six months later, January 14, 1941, a right Caldwell Luc operation was performed and tumor of the right maxillary antrum was found to extend into the orbit, ethmoid, lateral wall of nose and peritonsillar region. After this intervention, transitory cerebrospinal rhinorrhea with signs of meningeal irritation developed, but this subsided after sulfanilamide therapy. The patient returned to the hospital in July, 1942, complaining of severe right temporal headaches. Examination revealed no change in her neurologic and roentgenographic findings, but re-exploration disclosed a recurrent tumor and a small subtemporal epidural abscess which apparently originated from a chronic otitis media. The entire observed duration of the disease was more than 17 years.

CASE 7. Dagmar T., U. of Michigan Hospital, No. 309608, female, aged 20 years, was referred by Dr. K. B. Babcock, Detroit, Michigan. Patient had an osteochondroma of the left frontoethmoidal region, with 4 months' history. Operation was done with apparently total removal of tumor spreading to the anterior cranial fossa and paranasal sinuses. Small subcutaneous recurrence was removed 4 months later. There were signs of intracranial recurrence after 3 months. A third operation revealed sarcomatous recurrence infiltrating the scalp, dura, and brain, with extension to the nasal cavity. Death resulted from meningitis, 1 month after last operation. No autopsy was performed.

Four months prior to admission, the patient noticed a swelling on the left side of the forehead which was associated with dull headache, and later on, with diplopia. Biopsy of the lesion elsewhere showed the tumor to be a chondroma. After deep x-ray therapy, the neoplasm began to grow more rapidly.

Examination showed the following: There was a tumor the size of an orange, at the left side of the forehead, supraorbital ridge, and bridge of the nose. The mass, which had the consistency of hard rubber, was firmly attached to its bony base. The overlying skin was intact and not tender to pressure. The tumor displaced the left eye downward and outward, and caused slight edema of the left upper lid. There was also exopthalmos on the left (left eye 20 millimeters; right eye 13 millimeters). The left superior rectus and inferior oblique were paretic. Examination of the left fundus revealed retinal detachment in the region of the superior temporal vessels and venous engorgement.

Roentgenograms of the skull revealed a neoplasm eroding the left frontal bone, the frontal sinuses (especially the left one), the ethmoids, and the roof and medial wall of the left orbit. Extensive calcifications were present within the tumor (Figs. 4, b and c).

Diagnosis: Osteochondroma (or osteochondrosarcoma) of the left frontal and ethmoidal bones with intranasal, orbital, and intracranial extension.

Operation was performed on April 14, 1933, under ether anesthesia, by Dr. M. M. Peet. After a large frontal scalp

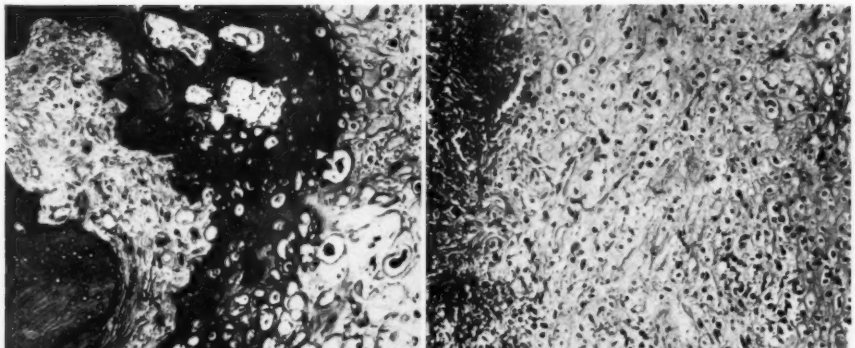


Fig. 6. Histological sections from a malignant osteochondroma, Case 7. a, left, Specimen from first operation shows relatively benign osteochondroma. b, Specimen of recurrent tumor, obtained by third operation, shows sarcomatous change (myxochondrosarcoma.)

flap had been turned down, a lobulated whitish tumor was exposed, covered by pericranium. The lower portions of the frontal bone were rongeured away to further expose the neoplasm which completely filled the frontal sinuses. On the left side, the tumor had destroyed the frontal bone, forming a large mass outside and a still larger mass inside of the bone, displacing the dura posteriorly. The neoplasm was firmly attached to and infiltrating the cribriform plate and extended into the ethmoid cells. The inner walls of both orbits were involved, especially on the left. After removal of all visible tumor, the widely opened nasal cavity was closed by an iodoform pack. A tear of the orbital dura which could not be sutured had to be covered by another iodoform pack.

Histologic report: The tumor was an osteochondroma with calcareous concretions in a myxomatous stroma. The neoplasm was regarded as not sufficiently cellular to cause metastases, but likely to recur and infiltrate locally (Fig. 6, a).

The postoperative course was complicated by transient cerebrospinal rhinorrhea and by severe epistaxis which was eventually controlled by ligation of the left external carotid artery.

The patient returned to the hospital 4 months later with recurrent tumor. A neoplasm, the size of a walnut, which infiltrated the skin as well as the dura, was removed. Histologic examination showed that the growth had become increasingly cellular, and had penetrated the dura, and that the involved corium of the skin contained sarcomatous areas. Thereupon the patient was given a course of deep x-ray therapy (600r).

Three months thereafter, she returned with signs of intracranial recurrence and was again operated upon by Dr. Peet, on November 25, 1933. The recurrent tumor infiltrated the skin, dura, and frontal lobes and had extended far into the nasal cavity. It was excised together with the tumor-infested skin, dura, and frontal cortex. The wound was packed and only partially closed. It was hoped that the large defect would eventually heal by granulation. Patient did fairly well for 3 weeks, but then developed meningitis leading to her death on December 24, 1933, approximately 1 year after the onset of the disease. Autopsy was not obtained.

The last surgical specimen showed that the neoplasm had become definitely sarcomatous in character (Fig. 6, b).

ANATOMICAL AND PATHOGENETIC CONSIDERATIONS

From the observations here noted and the cases reported in the literature, it is evident that the base of the skull is a preferential location of osteochondromas. When verified by operation or autopsy, these tumors often are found to be so large that it may be difficult or even impossible to ascertain their exact site of origin, yet the clinical course may be helpful in reconstructing the stages of anatomic evolution even in advanced cases.

In the first group, *primarily intracranial tumors*, there are 5 examples in our series. Four of these (Cases 1, 2, 3, and 4) are almost identical with the four observations reported by Hirschfeld, Levitt, Green and Childrey, and Paleari. In all 8 instances the osteochondroma originated from the sphenoid bone and protruded intracranially

in the posterior parasellar region. It was attached to one side of the clivus and the corresponding posterior clinoid process (Fig. 3, a) and spread to the base of the greater sphenoidal wing and adjacent bone by expansion rather than by actual invasion (Case 3). At first, the growth was entirely extradural, but later it protruded into the cranial cavity by penetrating the dura (Case 1). Leptomeninges and brain were indented and displaced, but not invaded.

The fifth case in our first group (Case 5) must be given special consideration since the basal osteochondroma was but one manifestation of generalized chondromatosis. There are two similar observations recorded in the literature (Clark, Lupo), but the validity of these appears dubious, because they were not verified. The objection might be raised here that localization at the base of the skull is merely incidental in general chondromatosis, yet it cannot be overlooked that in all 3 instances the chondroma of the sphenoid represented the *only* cranial localization.

In the second group, *primarily extracranial tumors*, there are 2 examples in our series (Cases 6 and 7). In these 2 cases, and in similar observations reported by Torrigiani, Wolf and Echlin, Menne and Frank, and others, the tumor arose in the sphenoidal or ethmoidal region and developed mainly in an extracranial direction; at an advanced stage, however, it also invaded the cranial cavity. Thus in Case 6, the osteochondroma presumably originated unilaterally in the posterior parts of the ethmoid and was first detected in the corresponding maxillary antrum. Later on the neoplasm spread through the ethmoidal cells and sphenoidal sinus to the other side where it penetrated the base of the skull in the parasellar area. Case 7 is an example of a more anteriorly placed lesion which developed in the frontoethmoidal area and invaded the orbit, the upper parts of the nasal cavity, and the floor of the anterior cranial fossa. In this instance the malignant (sarcomatous) character of the lesion was demonstrated by infiltration of scalp and brain. A similar case was described by Menne and Frank. In Torrigiani's patient the chondroma apparently originated in the sphenoidal sinus and extended intracranially, thus destroying the sella turcica. Wolf and Echlin briefly mention an observation at autopsy of a large chondroma of the sphenoidal region, extending into the nasopharynx.

The pathogenesis of basal osteochondromas is revealed by their characteristic site. It is highly probable that these tumors develop from residuals of the cartilaginous primordial cranium. Embryonic cartilaginous rests with future neoplastic propensities may be retained, either in suture lines or in areas between centers of ossification. Thus, one may expect foci of neoplastic growth at the junction of the sphenoid body with the greater wing of the sphenoid and petrous apex (Cases 1, 2, 3, and 4), or at the junction of the ethmoid with the sphenoid body (Case 6), or at the frontoethmoidal border (Case 7). It is also conceivable that chondromas may arise from heterotopic cartilaginous material within the mucous membranes of the paranasal sinuses.

The pathogenesis of basal osteochondromas should not be discussed without mentioning their relationship to the chordomas. The latter variety of tumor is derived from the notochord, a forerunner of the embryonic (cartilaginous) axial skeleton. It is interesting to note that chordomas are found in a location similar to that of osteochondromas, viz. at the junction of the basisphenoid with the basiocciput.

The histologic picture of basal osteochondromas is generally characteristic, although it may exhibit considerable variations. Some neoplasms are almost entirely composed of mature cartilage (chondroma), others contain elements of adult or embryonic mesenchymal tissue (fibrochondroma, myxochondroma, respectively) (Fig. 5, b). As a rule, areas of ossification are present (osteochondroma—Figs. 5, a and 5, c) and also degenerative changes such as calcification or mucinous degeneration. Some chondromas are acellular and noninfiltrative, others are highly cellular, poorly differentiated, and grow in a malignant fashion (chondrosarcoma—Case 7). Occasionally, a relatively benign osteochondroma may undergo progressive anaplastic differentiation into a malignant osteochondrosarcoma (Case 7, Figs. 6, a and b).

CLINICAL AND DIAGNOSTIC CONSIDERATIONS

Incidence and duration of symptoms. Basilar osteochondromas occur possibly more often in the female sex, but the number of observations is too small to permit accurate statistical evaluation. As a rule, these neoplasms become clinically manifest in young adults, between the ages of 20 and 30. Their rate of growth is slow, hence a clinical course over 10 or even 20 years is not unusual. If, on the other hand, the tumor becomes malignant, the course is likely to be rapid (1 year in Case 7).

Neurologic symptomatology. The intracranial osteochondroma of the sphenoid produces a characteristic clinical syndrome. As a result of the parasellar location of the lesion, the structures in the wall of the cavernous sinus are affected at an

early stage. Pareses of the 3d, 4th, 5th, and 6th cranial nerves are nearly always demonstrable. The lesion of the oculomotor nerve may remain incomplete and spare the medial rectus and the levator palpebrae superioris. Neuralgic pains in the distribution of the ophthalmic division and diminution of corneal reflex are early signs of trigeminal involvement. Sensory loss is usually most marked in the first trigeminal division and least in the third division, but when the tumor has attained a large size and compresses the gasserian ganglion, all trigeminal branches including the motor root may be equally affected. Sharp trigeminal pains should be differentiated from the duller and throbbing headaches elicited by irritation of the highly sensitive dura of the base and the cavernous sinsus. This dural pain is referred to the ipsilateral forehead, temple, occiput, and behind the eye. Its frequent association with nausea and vomiting (in Case 4) probably is a local meningovagal reflex phenomenon and should not be interpreted as evidence of increased intracranial pressure. In fact, basal osteochondromas rarely produce definite signs of increased intracranial pressure, and if so, only in the advanced stage. This is explained by the slow growth rate and the extradural location of these neoplasms. Since venous return to the cavernous sinus is mechanically impaired by the tumor, thrombotic processes may occur, an event which is indicated by sudden increase of cranial nerve involvement, exophthalmos, local edema, and venous stasis of eyelids. Sooner or later, the optic pathway also becomes implicated. Depending upon the direction of neoplastic growth, optic nerve, chiasm, or optic tract may suffer from local pressure. In more anteriorly placed lesions, a chiasmal syndrome with optic atrophy is likely to develop at an early stage (Case 5). In tumors extending more posteriorly and upward, homonymous hemianopsia, due to compression of the optic tract, may result (Case 1). Large osteochondromas inevitably encroach upon the hypophysis and its stalk, the hypothalamic region, the mesial portion of the temporal lobe, and the cerebral peduncle. Correspondingly, a pituitary-hypothalamic syndrome may develop and can be recognized by the presence of obesity, polyuria, polydipsia, impotentia, or amenorrhea, and drowsiness (as in Case 1 and in the observations of Paleari and Torrigiani). In two of our observations (Cases 2 and 3), peculiar attacks were noted, characterized by vegetative (parasympathetic) phenomena, undescribable sensation of fear without lowering of consciousness. These seizures might have been convulsive equivalents and evoked either by hypothalamic stimulation ("autonomic epilepsy") or perhaps by hippocampal discharge (atypical uncinate attacks?). Signs referable to compression of the cerebral peduncles are usually slight and clinically recognizable by minimal contralateral hemiparesis with increased deep reflexes. At an advanced stage, the expanding osteochondroma extends through the incisura tentorii into the posterior fossa causing pareses of the 7th and 8th cranial nerves (Cases 2 and 3).

Primarily extracranial osteochondromas of the ethmoidal or sphenoidal regions produce neurologic signs only in the later phases of the disease. At first, the symptomatology is rather uncharacteristic and indicative of an expansive or obstructive lesion of the paranasal sinuses. The neoplasm may become directly visible by rhinoscopy. Mucoceles, infections of the occluded sinuses, dacryocystitis and orbital cellulitis are occasional complications which obscure the clinical picture. If the tumor invades the orbit, the eye bulges and is displaced downward and outward, thus accounting for diplopia and blurred vision. When the neoplasm finally penetrates into the cranial cavity, the optic nerve is the first structure to become affected. This is manifested by signs of retrobulbar neuritis and, later, by optic atrophy and blindness. Posterior extension of the tumor through the pterygopalatine fossa and superior orbital fissure toward the parasellar region will produce involvement of the 3d, 4th, 5th (first and second divisions), and 6th cranial nerves.

Roentgenographic signs. The presence of basal osteochondromas is revealed by localized erosion of bone combined with dense calcifications in the tumor (Figs. 1, 2, and 4). Intracranial sphenoidal osteochondromas produce more or less marked parasellar erosion, i.e., unilateral destruction or thinning of clinoid processes, and sometimes also erosion of the mesial portion of the lesser sphenoidal wing and of the petrous apex (Cases 3 and 4). Ethmoidal osteochondromas may destroy ethmoidal bones, the floor of the anterior fossa, and the medial wall of the orbit (Case 7). Calcifications in osteochondromas are either arranged in coarse flakes (Figs. 1,a, b and 4, b, c) or they may be so dense as to simulate cancellous bone, thus outlining the entire tumor mass (Figs. 2, a, b).

Diagnosis. The diagnosis of osteochondroma arising from the base of the skull can be made before operation. Since parasellar lesions produce a characteristic clinical syndrome, they can be accurately localized, but it may be more difficult to ascertain the pathological type of the lesion present. The following conditions must be differentiated from the osteochondroma:

1. The subclinoid (parasellar) aneurysm of the internal carotid artery may be associated with similar neurologic signs,[1] but its history is usually shorter and the onset of symptoms more abrupt; furthermore it is likely to occur in older individuals. Calcified aneurysms show smooth round contours, sometimes only a semicircular line of calcification. The differential diagnosis can be made with certainty by arteriography.

2. Parasellar meningiomas, arising either from the anterior clinoid process, lateral wall of cavernous sinus or gasserian sheath ("gasseropetrosal meningiomas") are apt to cause earlier and more marked visual changes: Meningiomas of the inner portion of the lesser sphenoidal wing and anterior clinoid process produce early ipsilateral optic atrophy with visual field changes, later on a Foster Kennedy syndrome; gasseropetrosal tumors cause bilateral papilledema. Basal meningiomas often show localized hyperostoses at the point of their attachment, but they are less frequently calcified than chondromas. Calcareous shadows in meningiomas are usually finer and more uniform than those present in osteochondromas.

3. Craniopharyngiomas occur in patients of a younger age than do osteochondromas. They nearly always affect the optic pathways and the hypophyseal-hypothalamic area, and commonly produce signs of increased intracranial pressure, but encroach less often on other cranial nerves. Roentgenologically, they are characterized by intrasellar or extrasellar, but not parasellar erosion and by fine granular intrasellar or suprasellar calcifications which, as a rule, lie in the midline.

4. Chordomas may exhibit a symptomatology resembling that of osteochondromas. Their course is shorter, however, with a greater tendency to affect cranial nerves bilaterally and to invade the posterior fossa. These tumors may lead to considerable destruction of bone but do not calcify.

Primarily extracranial osteochondromas cannot be differentiated clinically from other neoplasms invading the base of the skull and paranasal sinuses, but their characteristic roentgenographic appearance may permit an anatomic diagnosis.

TREATMENT AND PROGNOSIS

Treatment. Since osteochondromas do not respond to radiation, surgical treatment is the only promising form of therapy. Primarily intracranial osteochondromas must be dealt with by neurosurgical methods. Unfortunately, it is rather difficult to expose the posterior parasellar region from which most of these tumors arise. An extradural subtemporal approach, as is customary in trigeminal rhizotomy, rarely affords sufficient exposure, unless the lesion is small. The usual exploration of the pituitary region by a frontal osteoplastic flap is likewise inadequate, since it permits inspection only of the anterior parasellar area. Much better access to the parasellar region is obtained by a low frontotemporal osteoplastic craniotomy combined with subtemporal decompression. Since intracranial pressure is usually not high, the outer margin of the lesion may be disclosed by intradural elevation of the temporal lobe, but hardly sufficient room is obtained in this manner for safe and complete removal of the neoplasm. It is, therefore, advisable to resect the anterior and inferior parts of the temporal lobe to uncover the deep seated tumor (Figs. 3, b and c). Technical difficulties of the operation are caused by the extradural and intradural expansion of the tumor, and by its intimate relationship to various cranial nerves, cavernous sinus, and to the internal carotid artery. Although the neoplasm itself may be completely avascular, detachment from its base may cause considerable hemorrhage, mostly from the middle meningeal artery and from venous radicals of the cavernous sinus and superior petrosal sinus. Most osteochondromas are easily broken up during removal, due to their brittle consistency. This facilitates their piecemeal removal, but it also increases the likelihood of incomplete extirpation. It is almost unavoidable that attempted radical removal of these tumors should be followed by at least a temporary increase of cranial nerve palsies (Cases 1, 2, and 3).

In primarily extracranial osteochondromas of the ethmoid of sphenoid, rhinologic methods of treatment are indicated and complete eradication possible, as long as they are small and confined to the paranasal sinuses. Large neoplasms, however, with extensive involvement of the orbit and intracranial cavity offer a very poor operative prospect. Combined intracranial and nasal approach was attempted in Case 7 and afforded a good exposure of the lesion. It should be mentioned that such an operation inevitably establishes a wide communication between the nasal and intracranial cavities with all its dangerous consequences, such as postoperative cerebrospinal rhinorrhea and ascending meningeal infection. On the other hand, the use of sulfonamides has considerably lessened the peril of these dreaded complications at the present time.

[1] In Case 4 the lesion was mistaken for an aneurysm, before definite changes were visible in the roentgenogram.

Prognosis. It was stated that the life expectancy of basilar osteochondromas may be a long one even without operation. In fact, the rate of growth may be so slow that the neoplasm appears to be stationary (Case 2). In most patients, severe headaches, trigeminal pains, or visual disturbances necessitate the operation at an early stage. Eventual recurrence may take place, because it is technically impossible to extirpate these tumors *in toto*, yet the patients may gain a long period of symptomatic relief from the operation. The outlook is most unfavorable in cases of extensive intracranial and extracranial involvement, since such lesions can be only partially removed and are liable to cause various distressing complications (sinus infections, dacryocystitis, and orbital cellulitis, etc.—Case 6).

SUMMARY

Seven cases of osteochondroma arising from the base of the skull are reported. In 4 almost identical cases, the lesion originated extradurally from the sphenoid bone and protruded intracranially in the posterior or parasellar region. In the fifth case, the extradural tumor of the sphenoid was the only cranial manifestation of osteochondromatosis. In Cases 6 and 7, the neoplasm originated extracranially in the ethmoidal region, invaded paranasal sinuses, and finally extended into the cranial cavity.

The sphenoid and ethmoid are preferential sites of osteochondromas. These lesions develop apparently from cartilaginous rests of the primordial cranium. Their relationship to the chordomas is mentioned. The histologic picture of osteochondromas is described with its variants.

Because of the slow rate of growth, the clinical course of osteochondromas is usually long, often lasting more than a decade. They occur in young adults and are possibly more common in the female.

Intracranial osteochondromas in the parasellar region produce a neurologic syndrome typical for this location. Primarily extracranial osteochondromas show signs of an expanding lesion in the paranasal sinuses and cause neurologic manifestations only at an advanced stage.

Roentgenograms of basal osteochondromas are almost pathognomonic and are characterized by a combination of bony erosion and heavy calcification.

The differential diagnosis of parasellar osteochondroma is discussed.

The osteochondromas of the base of the skull require surgical treatment. Tumors of the intracranial parasellar variety are best exposed by frontotemporal osteoplastic craniotomy combined with subtemporal decompression, after partial resection of the temporal lobe. Extracranial osteochondromas extending into the paranasal sinuses may, if small, be successfully operated upon by the rhinologic methods. Large lesions with intracranial extension must be attacked by a combined intracranial and nasal approach which may result in complications such as cerebrospinal rhinorrhea and ascending meningitis. Since most intracranial osteochondromas must be removed piecemeal, their extirpation may be incomplete and hence a recurrence is likely to develop eventually. The postoperative period of survival may be a long one, unless the neoplasm has sarcomatous propensities.

REFERENCES

1. Chorobski, J., Jarzymski, J., and Ferens, E. Surg. Gyn. Obst., 1939, 68: 677–686.
2. Clark, L. P. J. Nerv. Ment. Dis., 1907, 34: 596.
3. Green, M. I., and Childrey, J. H. J. Nerv. Ment. Dis., 1939, 89: 650–652.
4. Hickey, H. L. Arch. Otolar., 1940, 31: 645–652.
5. Hirschfeld, L. C. rend. Soc. biol., 1851, 3: 94–96.
6. Levitt, J. M. Arch. Ophth., 1934, 12: 877–886.
7. Lupo, M. Riv. otoneur., 1925, 2: 152–157.
8. Menne, F. R., and Frank, W. W. Arch. Otolar., 1937, 26: 170–178.
9. Paleari, A. Riv. otoneur., 1938, 15: 59–71.
10. Torrigiani, C. A. Riv. otoneur., 1923–1924, 1: 265.
11. Wolf, Abner, and Echlin, F. Bull. Neur. Inst. N. York, 1936, 5: 515–525.

THE RESULTS OF NEPHRECTOMY ON EXPERIMENTAL RENAL HYPERTENSION

HENRY S. PATTON, M.D., ERNEST W. PAGE, M.D., and ERIC OGDEN, M.R.C.S.,
Berkeley, California

DURING the past 6 years there has been considerable interest in the relationship between unilateral renal disease and arterial hypertension in man, and numerous efforts have been made to modify that hypertension by removal of the diseased kidney. Undoubtedly the impetus for this clinical approach has been the studies of experimental renal hypertension initiated by Goldblatt and his group who demonstrated that permanent hypertension results from interference to the renal blood supply. Shortly afterward, scattered case reports appeared in which nephrectomy was followed by a cure of the hypertension. Subsequent reports by urologists have been numerous and the results variable. In 1941, Abeshouse (1), in an extensive review, summarized the literature on hypertension and unilateral renal disease.

REPORTED CLINICAL RESULTS

Using part of this collected data (2), we have prepared a table showing the end-results of nephrectomy on those forms of hypertension presumably originating from a single diseased kidney. This is not a complete compilation of all reported cases, but represents a very large sampling.

Table I presents the type of unilateral renal disease associated with hypertension and the number of cases studied after unilateral nephrectomy. The results are tabulated under 3 headings which might be termed in effect "failures," "improved," and "cured." It is evident at first glance that the results vary according to the type of kidney disease. It is not statistically sound to present totals on such a miscellaneous collection of cases; nevertheless, such totals give an indication of the trend of the results obtained and furthermore enable us to compare the clinical results with the experimental results which we present below. It will be noted that approximately one-fourth of all of the reported cases resulted in a complete relief of the arterial hypertension, but that in over half of the cases there was either no lowering of blood pressure or a continuation of the rise following extirpation of the diseased kidney.

A few of the failures may be due to the fact that the hypertension was independent of the renal disease; in others there may have been a coexisting disturbance of circulation in the remaining kidney. Furthermore, even though the remaining kidney was shown to be normal by the usual kidney function tests and appeared to be normal following a thorough urological study, it is recognized that experimental renal hypertension may exist in animals with normal clearance values (6) and that there may be "silent" parenchymal renal lesions in man. In the majority of instances the residual hypertension following removal of the diseased kidney has been unexplained.

EXPERIMENTAL INVESTIGATION

Our experiments were designed to answer several questions bearing upon this problem: (1) In hypertension produced experimentally by unilateral partial ligation of the renal artery, what are the end-results of removing the affected kidney and how do these results compare with the clinical reports? (2) What are the factors that determine the success or failure of nephrectomy in curing the hypertension? (3) Does the hypertension resulting from the unilateral disease produce irreversible changes in the opposite kidney? (4) If so, is it the severity of the hypertension or its duration that causes the greatest damage?

The rat, sheep, and goat are the only known species except for man in which unilateral renal damage may result in permanent hypertension. Unlike dogs, rabbits, and monkeys, in which unilateral renal ischemia produces a transient hypertension only, some of our observed rats with unilateral partial renal artery ligation have had a permanent hypertension for a year and a half, and this period of time represents over half of the usual lifetime of the animal. For these reasons, the rat was chosen for our experimental observations.

Methods. In young adult rats of both sexes the left renal artery was partially occluded by a silk

From the Division of Physiology and the Department of Obstetrics and Gynecology, University of California Medical School.
Supported by a grant from the John and Mary Markle Foundation.

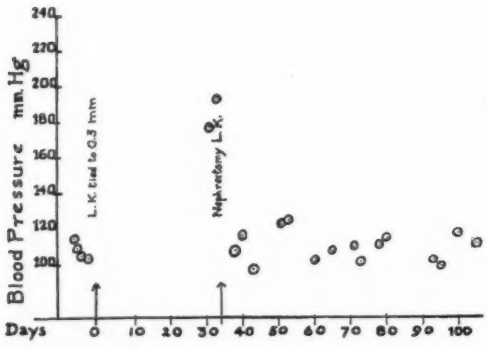


Fig. 1. Complete relief of hypertension of short duration.

ligature, the technique of Wilson and Byrom being used (13). Blood pressures were followed two or three times a week by the tail plethysmograph method of Williams, Harrison, and Grollman. After the hypertension had developed and was moderately well stabilized, the left kidney was removed and the blood pressure followed for a period of several weeks. The excised kidney was preserved in Bouin's fluid for histological study. In many animals the quantitative urinary output of albumin was checked before and after the nephrectomy. The animal was finally sacrificed, the weight of the heart obtained, and various tissues saved for a histological study of the vascular system.

Results. The initial preoperative blood pressures of our normal rats ranged from 100 to 120 with a mean of 110. We considered any rats hypertensive when two or more consecutive readings were over 140 millimeters or in which the average value of all of the readings following the operation was over 130 millimeters. In the study of several hundred rats, we have never found a sustained spontaneous hypertension. Some of the animals we operated upon developed a hypertension of over 200 millimeters systolic pressure.

Table II shows the results of the nephrectomy in relation to the duration of the hypertension and also in relation to its severity. The severity of the hypertension had little to do with the success of the nephrectomy, but the duration did. Any level of hypertension of less than 10 weeks was usually markedly improved or reduced to normal by removal of the affected kidney. Two weeks in the life of a rat is roughly comparable to 1 year in man.

Charts 1, 2, and 3 illustrate sample protocols on typical experiments.

Two groups of independent workers have recently reported similar observations on rats. Wilson and Byrom (14) produced hypertension in 27 rats by applying a small silver clip to one renal artery, and they studied the results of removing that kidney. Friedman, Jarman, and Klemperer (3) applied a cellophane bag to one kidney, thus producing a perinephritis and this resulted in sustained hypertension in a group of 44 rats. Table III presents a summary of all of the reported results.

In spite of differences in technique, it will be noted that the results are similar. The totals are

TABLE I.—THE THERAPEUTIC EFFECTIVENESS OF NEPHRECTOMY IN CLINICAL HYPERTENSION

Type of unilateral renal disease associated with hypertension	Number of patients having nephrectomy	Effects on hypertension			
		No change or a rise	Definite lowering but not to normal	Sustained return to normal	
				No.	Per cent
Pyelonephritis	41	14	5	22	53
Tuberculosis	18	5	3	10	56
Chronic inflammatory disease complicated by calculus	112	87	5	20	16
Unilateral hydronephrosis	38	17	7	14	37
Neoplasm	21	15	5	1	4
Congenital hypoplasia of one kidney	3	0	0	3	100
Totals	233	138	25	70	
Per cent		60	10	30	

TABLE II.—THE RELATION OF DURATION AND SEVERITY OF HYPERTENSION TO THE EFFECTIVENESS OF NEPHRECTOMY IN RATS

Duration—wks.	No. of animals	Result of nephrectomy		
		No change or a rise	Lowered, but not to normal	Return to normal
5–10	21	2	9	10
11–45	26	13	11	2
Totals	47	15	20	12
Severity of hypertension—mm.				
140–160	26	12	9	5
161–180	11	2	6	3
181–200	7	1	3	3
Over 200	3		2	1
Totals	47	15	20	12

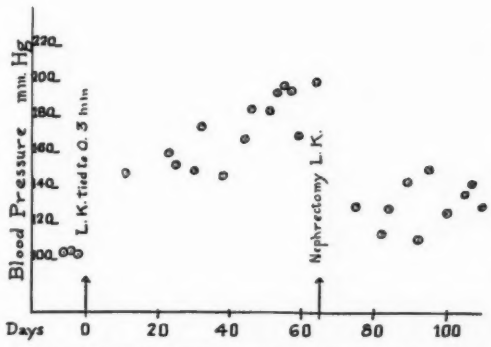


Fig. 2. Moderate improvement of hypertension of 2 months' duration.

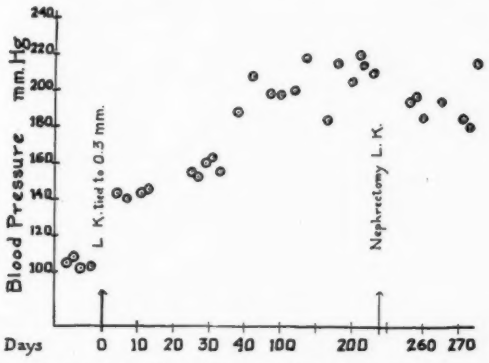


Fig. 3. No lowering of hypertension of 7 months' duration. (Time scale has been altered to conserve space.)

presented in Table III and the very close similarity between the results obtained by nephrectomy in all the clinical cases reported (compare with Table I) and the results obtained by nephrectomy in hypertensive rats by three groups of workers would seem to indicate that the nature of the residual hypertension in both rats and in man is the same. Thirty per cent of human cases and 29 per cent of rats were completely relieved by nephrectomy.

We observed one interesting fact which is readily explained. In some of the animals, the left kidney to which the blood supply had been reduced by operation became progressively atrophied until at the time of its removal there was nothing left but a small calcified nodule. Removal of this mass did not lower the hypertension in a single instance. These nodules had once been small, pale kidneys which secreted the renal pressor substance and caused hypertension and, in turn, had resulted in damage to the opposite kidney. If subsequent atrophy with complete loss of blood supply to the affected kidney failed to cure the hypertension, it is obvious that surgical nephrectomy would accomplish no more. In other rats even though the renal artery was found to be completely occluded, there was a small pink area at the inferior pole of the kidney supplied by the spermatic or ovarian branch of the ureteral artery, and nephrectomy in these animals often lowered the blood pressure.

Pathological observations. During life, large amounts of albumin were excreted by the hypertensive rats, but the amounts did not parallel the severity of hypertension. Following nephrectomy, there was no consistent change in the albuminuria, indicating that most of the protein leaked through the glomeruli of the intact kidney.

Cardiac enlargement, from 10 to 50 per cent above the expected weight, was observed on all rats still hypertensive at the time of death. The increase in heart weight was quite closely proportional to the level of blood pressure at the time of death. In view of the invariability with which such enlargement is noted, it is interesting to observe that the heart weight was normal in those rats "cured" by nephrectomy, even though the blood pressure had once been at very high levels. This establishes the reversibility of cardiac hypertrophy.

Histological examination of the kidneys[1] showed a number of pathological changes similar to those seen in human hypertensive disease. In the left kidneys which had been removed surgically, there

[1]We are indebted to Mr. E. Johnson and Mr. R. Bazzanella for preparation and special staining techniques, and to Dr. David Singman for interpretation of the renal changes.

TABLE III.—COLLECTED RESULTS OF NEPHRECTOMY ON EXPERIMENTAL HYPERTENSION IN RATS

Authors	Method of producing hypertension	Number	Result of nephrectomy		
			No change or a rise	Lowered, but not to normal	Return to normal
Wilson and Byrom	Silver clip obstructing one renal artery	27	8	9	10
Friedman, Jarman, and Klemperer	Cellophane bag around one kidney	44	3	29	12
Patton, Page, and Ogden	Partial occlusion with silk tie of one renal artery	47	15	20	12
Totals		118	26	58	24
Per cent			22	49	29

were large areas of necrosis due to anemic infarction together with relatively normal appearing tissue. The iron hematoxylin and analine blue stain revealed varying degrees of thickening of the glomerular capillaries. In some instances, there was a thickening of the arterioles, but in general the vascular changes in the ischemic kidney were not as marked as in the intact kidney.

The right kidneys, which had not been disturbed surgically, showed a varying degree of thickening of the walls of the arterioles with increased cellularity in all instances. There were no arteriosclerotic changes noted in the larger arteries. The parenchyma showed tubular dilatation and cloudy swelling. The glomerular capsules appeared thickened, and the glomeruli were quite cellular and showed a thickening of the capillary walls such as noted in cases of human eclampsia (8). In addition to the vascular changes, there were varying degrees of interstitial inflammation in some of the nonligated kidneys.

The pathological changes observed in these kidneys are quite identical with those described and illustrated by Schroeder and Neumann (10), who likewise studied the effects of arterial hypertension in rats. We agree with them, as opposed to the findings of Wilson and Byrom (13), that the kidney to which the blood supply was limited participates in the vascular changes. This may simply indicate that the mean intrarenal arterial pressure—apart from the pulse pressure—is the same on both sides in spite of the renal artery constriction.

EVALUATION OF STUDY

Our findings confirm the opinions of Weiss and Parker and of Wilson and Byrom (14), that unilateral renal disease sets up a vicious circle resulting in irreversible damage to the opposite kidney which then results in further hypertension, further renal damage, and so on.

In order to cure experimental renal hypertension in rats by nephrectomy, the disease should be of short duration and the renal lesion must be confined to one kidney, but must not have produced a total lack of function of that kidney. These criteria are similar to those derived from clinical observations on man by Schroeder and Fish (9) who set an arbitrary limit of 2 or 3 years for the duration of human hypertension if a satisfactory result from nephrectomy were to be expected. It is of interest that this period corresponds roughly to the percentage of life span which also holds true in rats. It seems that the rate of development of such pathological changes in the vascular system of rats is markedly accelerated.

As stated in a recent study of 193 nephrectomized patients by B. Friedman, Moschowitz, and Marrus (4) the decision to remove a pathological kidney should be based on the nature of the disease and not on the expectation of curing hypertension. If the opposite kidney were unexpectedly diseased, the nephrectomy might indeed precipitate a further increase in blood pressure. In 5 carefully studied cases, M. Friedman and his coworkers (5) determined the diodrast and inulin clearance before and after unilateral nephrectomy and in 3 cases demonstrated the feasibility of separate renal clearance determinations for each kidney. Unless this separate evaluation is done, no function test would furnish a positive clue as to the presence or absence of unilateral kidney disease.

Whether the damage to the normal kidney resulting in residual hypertension is caused by the hypertension *per se*, or by a toxic substance arising from the diseased kidney as suggested by the work of Winternitz is not clear, and our data sheds no light on this problem. The often confirmed observation that residual hypertension following the acute hypertensive states of pre-eclampsia and eclampsia depends more on the duration than the severity of the disease coincides with our conclusions.

SUMMARY AND CONCLUSIONS

The reported clinical cases of hypertension and unilateral renal disease in which a nephrectomy was done have been reviewed. In over half of these patients the blood pressure was not lowered or continued to rise following surgery.

This problem was studied on rats in order to determine the factors which influence the success or failure of nephrectomy in curing hypertension. Permanent high blood pressure was produced by obstructing the blood supply to one kidney, and this kidney was then removed after varying intervals of time. Like the results in man, half of our rats had no lowering of the blood pressure and only 20 to 30 per cent of the animals were cured of hypertension. In the animals with residual hypertension, albuminuria persisted, and a histological study of the remaining kidney revealed numerous vascular changes similar to those observed in human hypertension and apparently accounting for the continued maintenance of the high blood pressure. If the affected kidney had become completely devoid of a blood supply, its removal was a useless procedure. The greatest success following nephrectomy was in those animals with hypertension of short duration, and within the limits of our experiments, the severity of the hypertension was not of importance in determining the end-result.

REFERENCES

1. ABESHOUSE, BENJAMIN S. Surgery, 1941, 9: 942.
2. Idem. References 23, 32, 33, 38, 56, 62, 68, 119, 129, 143, 155, 156, 172, 183, 190, 200, 214, 250, 253.
3. FRIEDMAN, B., JARMAN, J., and KLEMPERER, P. Am. J. M. Sc., 1941, 202: 20.
4. FRIEDMAN, B., MOSCHOWITZ, L., and MARRUS, J. J. Urol., 1942, 48: 13.
5. FRIEDMAN, M., SELZER, A., KREUTZMANN, H., and SAMPSON, J. J. J. Clin. Invest., 1942, 21: 19.
6. FRIEDMAN, M., SUGARMAN, H., and SELZER, A. Am. J. Physiol., 1941, 134: 493.
7. GOLDBLATT, H., LYNCH, J., HANZAL, R. F., and SUMMERVILLE, W. J. Exp. M., 1934, 59: 347.
8. PAGE, E. W., and COX, A. J. West. J. Surg., 1938, 46: 463.
9. SCHROEDER, H. A., and FISH, G. W. Am. J. M. Sc., 1940, 199: 601.
10. SCHROEDER, H. A., and NEUMANN, C. J. Exp. M., 1942, 75: 527.
11. WEISS, S., PARKER, F., and ROBB, G. P. Ann. Int. M., 1933, 6: 1599.
12. WILLIAMS, J. R. JR., HARRISON, T. R., and GROLLMAN, A. J. Clin. Invest., 1939, 18: 373.
13. WILSON, C., and BYROM, F. B. Lancet, 1939, 1: 136.
14. Idem. Q. J. Med., Oxf., 1941, 10: 65.
15. WINTERNITZ, M. C., MYLON, E., and KATZENSTEIN, R. Yale J. Biol., 1941, 13: 595.

AN IMPROVED OPERATIVE METHOD FOR OBTAINING BONY FUSION OF THE GREAT TOE

D. H. O'DONOGHUE, M.D., F.A.C.S., and RICHARD STAUFFER, M.D., Oklahoma City, Oklahoma

FOR many years it has been the practice on the various services at the Crippled Children's Hospital to carry out an operative fusion of the interphalangeal joint of the great toe in all cases of transplantation of the extensor hallucis tendon to the dorsum of the foot.

It has been observed that bony fusion of this joint actually occurs in only a comparatively small percentage of these cases (Table II). Many patients develop a satisfactory fibrous fusion in good position and are pain free. Many others present no fusion at all, but the toe remains in good position, the handicap being difficulty in putting on socks and shoes due to instability of the toe. A certain other percentage (Table I), however, go on to flexion contracture of the toe with definite symptoms caused by resulting hammer toe; namely, corns, calluses, and inability to wear a shoe. Many of the patients, therefore, required a re-fusion of the toe, either because of pain or the inconvenience resulting from instability.

The usual method of arthrodesis of the interphalangeal joint was carried out in the majority of these patients. This procedure consisted of removal of the cartilage, careful approximation of the raw bone surfaces, and suture of the stub of the extensor hallucis attachment to the periosteum of the dorsum of the proximal phalanx. Plaster immobilization was carried out, usually incidental to whatever period of time the foot required immobilization; i.e., triple arthrodesis, some 3 months; tendon transplants, 3 to 6 weeks, etc. No specific fixation was applied other than the cast to the foot. In an analysis of a series of patients which we were able to follow at the clinic, it appeared that about 80 per cent of the patients did not get a bony fusion, and that 20 per cent required re-fusion because of the resultant flexion deformity or other complaints. For this reason, we felt it advisable to seek a more certain

From the orthopedic service of the Crippled Children's Hospital.

TABLE I.—CASES OF GREAT TOE FUSION WITHOUT WIRE FIXATION

No. Age	Initials Sex	Result
1 10	B.S. M*	Fibrous union with toe flexion deformity
2 16	B.B. M*	Fibrous union with toe flexion deformity
3 9	A.R. F*	Fibrous union with toe flexion deformity
4 7	W.C. F*	Fibrous union with toe flexion deformity
5 10	B.V. M	Bony union
6 6	W.W. M	Bony union
7 16	L.H. F	Fibrous union
8 12	N.R. M	Fibrous union
9 13	W.J. F	Fibrous union
10 6	E.D. M	Fibrous union
11 14	R.W. M	Bony union
12 5	V.C. M	Fibrous union
13 20	O.C. M	Fibrous union
14 13	R.H. M †	Fibrous union
15 19	K.B. M	Fibrous union
16 7	L.C. M	Fibrous union
17 12	G.J. F	Bony union
18 12	N.R. M	Fibrous union
19 18	W.C. M	Bony union
20 17	A.S. M	Fibrous union

*These toes required re-fusion because of flexion deformity.
†Mild postoperative infection; good clinical result.
Diagnosis was poliomyelitis in all cases. Immobilization consisted of plaster case for 3, 6, 12 weeks, depending on foot operation, i.e., tendon transfer, triple, etc.

20 per cent showed solid union, 80 per cent, non-fusion; 5 per cent infection; 20 per cent, flexion deformity.
(All cases included are from the orthopedic service of Crippled Children's Hospital.)

Fig. 1. Typical case showing flexion deformity following failure of fusion.

Fig. 2. Postoperative film, showing position of pin.

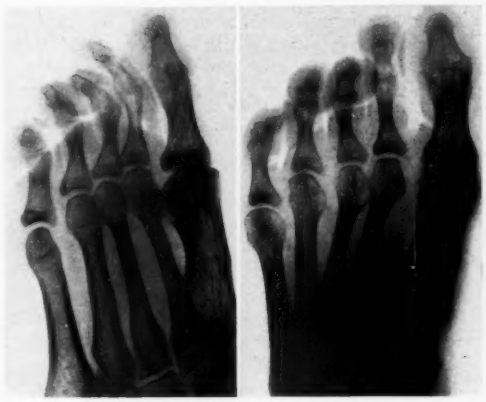


Fig. 3. Same case as Figure 2 showing bony union and removal of pin.

TABLE II.—CASES OF GREAT TOE FUSION WITH INTERNAL WIRE FIXATION

No. Age	Initials Sex	Time pin removed	Time of fusion	Results (x-ray)
1 10	B.S. M*	7 weeks	15 weeks	Bony fusion
2 16	B.B. M*	7 weeks	8 weeks	Bony fusion
3 9	A.R. F*	11 weeks	No fusion	Fibrous union
4 6	K.G. M	13 weeks	13 weeks	Bony fusion
5 7	W.C. F*	10 weeks	12 weeks	Bony fusion
6 7	I.M. F	7 weeks	16 weeks	Bony fusion
7 10	F.B. F†	14 weeks	No fusion	Fibrous union
8 9	C.B. M	16 weeks	16 weeks	Bony union
9 10	P.A. F	8 weeks	12 weeks	Bony union
10 17	V.E. F	Pin still in	12 weeks	Bony union
11 13	F.S. M	20 weeks	10 weeks	Bony union
12 10	L.V. F‡	17 weeks	12 weeks	Bony union
13 8	C.P. M‡	16 weeks	16 weeks	Bony union
14 25	D.G. F‡	12 weeks	18 weeks	Bony union

*Cases re-fused because of flexion deformity following original fusion operation.

†Complicated by infection of the distal phalanx. After curettement, good clinical result.

‡Private patients of D. H. O'D.

Diagnosis of all cases was poliomyelitis. Majority of cases from the orthopedic service of Crippled Children's Hospital.

85 per cent had solid bony fusion; 14 per cent, fibrous union, no deformity; 7 per cent, infection; none had flexion deformity.

method for fusion and so prevent this high percentage of poor results.

Taylor reported a method of fixation for the phalanx in treatment of hammer toe which seemed highly adaptable to this situation. Our present operative technique follows. Careful denudation of the cartilage surfaces of the interphalangeal joint is carried out with apposition of the raw bone surfaces. While the toe is held in satisfactory position, a Kirschner wire is drilled linearly through the end of the toe, traversing the distal phalanx, crossing the denuded joint, and extending well into the proximal phalanx. Ordinary closure is then carried out. Since the Kirschner wire provides such firm internal fixation, no external immobilization is necessary. Various methods of treatment of the end of the wire have been used, the most satisfactory being to clip it

off just outside of the skin surface. This permits easy removal and at the same time the wire is not left protruding enough to interfere at all with the sock or the shoe. Weight bearing is permitted as soon as the wound is healed, provided other conditions of the foot permit. Following adoption of this method of treatment bony fusion occurred in 85 per cent of the patients (Table II). Three patients developed slight serous drainage about the wire, which promptly healed following removal of the wire. The only complication of any note consisted of a localized osteomyelitis around one of the wires. This occurred when the patient accidentally kicked the wire back into his toe while going barefooted. (The wire had protruded too far.) On removal of the wire and curettement of the sinus, this condition healed promptly without solid fusion of the joint but with good clinical result. In one other patient of this series fusion failed; in this particular case, the wire was removed too soon. The patient obtained only fibrous union, but with a satisfactory clinical result. Since there seems to be no contraindication to leaving the wire in, under ordinary circumstances the wire is not usually removed until bony fusion is demonstrable by x-ray. Many of our patients wore the wire much longer than necessary due to the fact that they were having no difficulty and failed to return to the clinic at the designated time. The average time for leaving the wire in was 12 weeks, and it is probable that a somewhat longer period would be desirable provided there is no discomfort from the wires. All of the patients reported had poliomyelitis and were subjected to a transplantation of the extensor hallucis tendon to the dorsum of the foot.

CONCLUSION

A satisfactory method for obtaining solid fixation of the interphalangeal joint of the great toe, as herein described, in our hands has materially improved the result in arthrodesing operations of the interphalangeal joint of the great toe. This method was used initially in those cases in which bony fusion had failed to occur, but at the present time we are using it routinely on our service and are obtaining excellent results.

REFERENCE

TAYLOR, R. G. J. Bone Surg., 1940, 22: 608.

DUSTING POWDER GRANULOMAS FOLLOWING SURGERY

WILLIAM McKEE GERMAN, M.D., Cincinnati, Ohio

IT has been occasionally observed (7) that talcum powder, hydrated magnesium silicate, used so extensively and often so carelessly as a glove and dusting powder is capable of producing granulomas in tissue.

Feinberg has reported granulomas in the subcutaneous tissues of patients who had previously had thyroidectomies. Antopol has observed the lesions in a group of patients in whom the granulomas were produced by lycopodium spores, following the use of this material as a dusting powder; and has reported 1 case produced by talc. Here the lesions were found in the serosa of the appendix.

Ramsey and Douglas (8) have recently reported the finding of talc granulomas in various localities and caution against the use of the material in abdominal surgery.

That talc produces a form of peritoneal inflammation is attested by McCormick and Ramsey (6), and that silica can give rise to granulomatous masses which may be mistaken clinically for neoplasms has been shown in a report of such a mass developing in the scar from a scalp laceration (5).

Occasionally the pathologist is called into the operating room to have the surgeon point out small peritoneal lesions, some just visible to the naked eye, some as large as 2 millimeters in diameter. These may be on the appendix, the oviducts, the peritoneum of the uterus, or the coils of the intestine. There may be but a single lesion or there may be many. There is no free fluid in the abdomen and adhesions may or may not be present. The surgeon invariably suggests tuberculosis or carcinomatosis.

The lesions are discrete. A small aggregation of them may give the appearance of coalescence. They are covered by an intact layer of peritoneum unless they may be located within some adhesions (Fig. 1). There is no visible reaction of the surrounding tissues. The lesions escape notice in the ovaries (Fig. 2) and the omentum because of the irregular surface of these structures. They are occasionally seen on the surface of the liver if the previous surgical interference has been in this region. Inquiry reveals that every one of these patients has had a previous laparotomy.

From the Department of Pathology, College of Medicine, University of Cincinnati and the Department of Pathology, Good Samaritan Hospital, Cincinnati, Ohio.

Routine histological sections of the lesions show tiny granulomas consisting of one or a few giant cells, surrounded by a few lymphocytes and macrophages and a mild proliferation of histiocytes which may have the appearance of epithelioid cells. Even histologically some of the lesions may resemble tubercles and that some have been mistaken for tuberculous lesions is understandable (Fig. 3). Gardner has commented upon the similarity of tuberculous and silica lesions.

If the lesions are scrutinized carefully by the ordinary illumination, foreign body material may or may not be seen in them. But if polarized light be used, the silicate crystals will be seen to stand out in brilliant illumination as an electric sign in a night sky. Cellulose fibers from gauze and cotton behave in a similar manner (Fig. 4). Both of these substances, chemically inert, are quite likely to be unseen in routine sections with the usual source of illumination.

So useful is polarized light that we have come to use it routinely in all granulomatous and cicatricial lesions.

It has been our observation that if interval or serial sections are routinely taken through the omentum of patients previously operated upon and these sections are studied with polarized light, granulomas and crystals will almost always be found. The large number of crystals found in the omentum is due to the natural scavenger activity of the cells of that structure. It might be added that fragments of cellulose fibers from surgical sponges are likewise occasionally found where they too induce a similar type of foreign body reaction.

The frequency with which these granulomas are found in the serosal layers of the viscera and in adhesions has led us to speculate upon the relation between dusting powder and adhesions.

Prompted by the constant association of talc granulomas and adhesions in patients previously operated upon, the following two sets of studies have been made: (1) An analysis of 50 hospital patients presenting talc granulomas in various localities; (2) a study of such lesions produced experimentally in laboratory animals.

PATIENTS PRESENTING TALCUM GRANULOMAS

Fifty consecutive, unselected hospital patients previously operated upon and presenting talcum

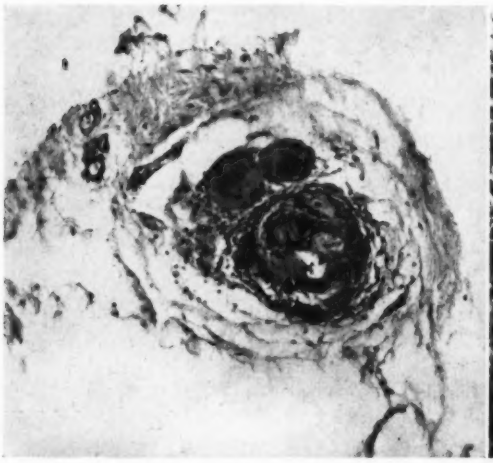


Fig. 1. Routine illumination. Granuloma with crystals and giant cells in tubal adhesions.

Fig. 2. Polarized light. Granuloma with crystals in cortex of ovary.

granulomas were subjected to careful study. The following points were noted in the study: (1) the patients' sex and age; (2) the symptoms for which the patient came to the hospital; (3) the date and type of present operation; (4) the number of previous operations; (5) the date and type of previous operations; (6) the presence, location, and amount of adhesions; (7) the macroscopic description of the surgical specimens; (8) the site of and an estimate of the number of talcum granulomas as shown by the histological sections which were made in each case.

The purpose of these studies was to correlate, if possible, the number of talcum granulomas, and therefore the volume of talcum, with the pathology seen in the abdomen and the amount of adhesions observed.

An analysis of the cases studied showed the following:

1. Sex and age had no bearing upon the pathology.

2. Every case had had a previous surgical operation of some type.

3. Of the 50 patients studied 42 had had 1 pre-

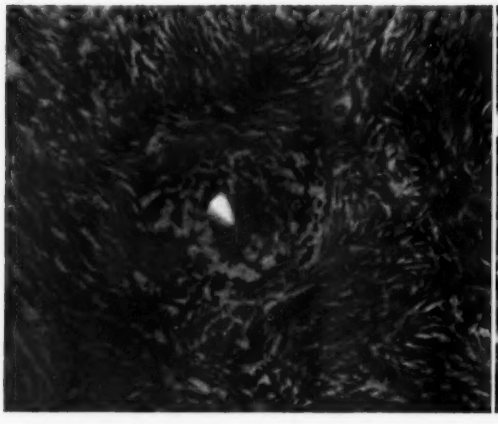


Fig. 3. Polarized light. Small granuloma in cortex of ovary with giant cell containing a large crystal. With ordinary illumination the lesion resembles a young tubercle.

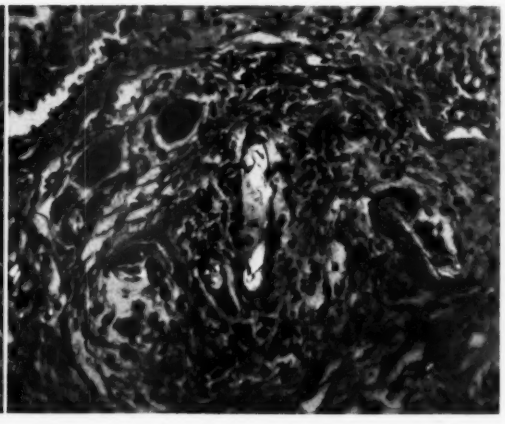


Fig. 4. Granuloma in appendiceal scar. By polarized light, this section is found to contain both cellulose fibers and talc crystals.

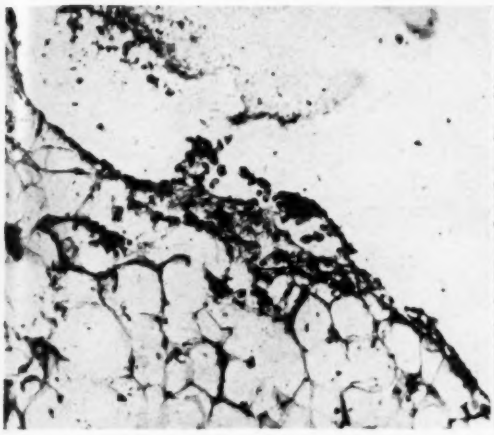


Fig. 5. Routine illumination. Talc crystals on contact with peritoneum are rapidly surrounded by proliferating serosal cells. Guinea pig; 24 hours.

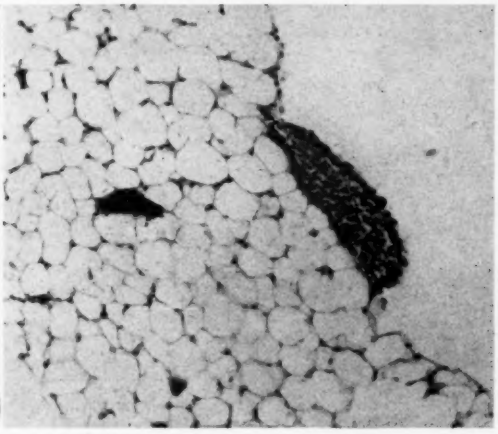


Fig. 6. Routine illumination. Talc crystals covered by an intact layer of serosal cells, forming young granuloma. Guinea pig; 48 hours.

vious operation; 7 had had 2 previous operations; and 1 patient had had 5 previous operations.

4. The time interval between the operations was of no apparent importance.

5. In so far as the information was available in the patients' records there was no apparent correlation between the symptoms and the talc. It was observed that some of the patients complained of the same symptoms for which they had originally sought relief.

6. In general it was observed that adhesions were more abundant in patients who had had more than 1 previous operation and that the more extensive the surgery the more abundant the ad ıesions.

7. Of the 50 patients presented, 40 showed intra-abdominal granulomas.

8. Forty-one patients were women, who are more often the victims of surgery than men (often useless surgery).

9. Every patient showing intra-abdominal granulomas also showed adhesions. There was a constant association between the presence of silicate and adhesions.

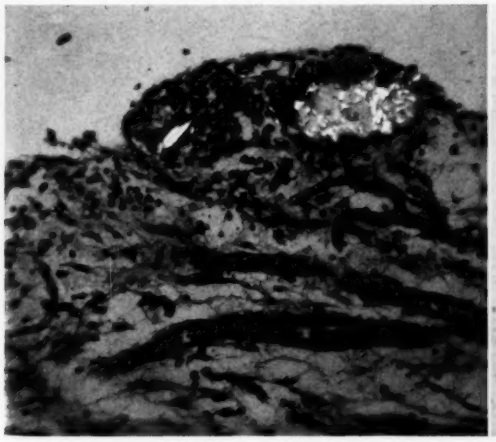


Fig. 7. Polarized light. Talc crystals shown in young granuloma, covered by intact layer of serosal cells.

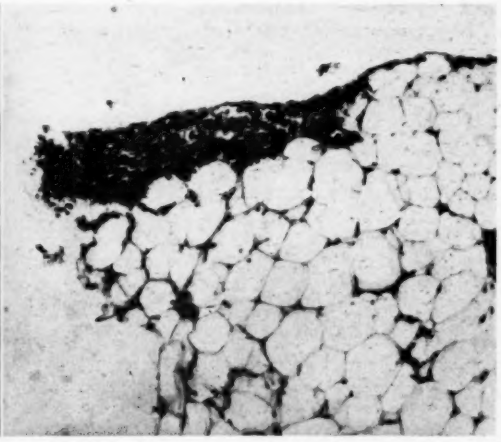


Fig. 8. Routine illumination. Young granuloma sinks to plane of surrounding serosa.

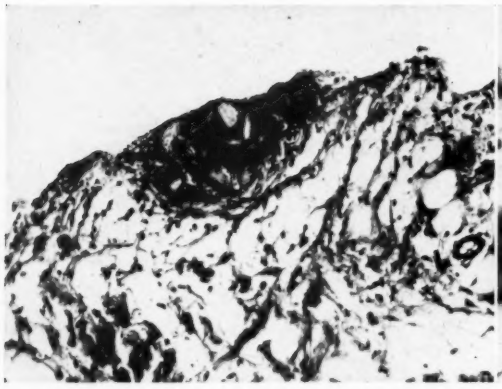


Fig. 9. Polarized light. Young peritoneal granuloma containing crystals. It has sunk to plane of serosa and is covered by an intact layer of serosal cells.

Fig. 10. Polarized light. Peritoneal granuloma, late, containing giant cells which contain the crystals. Lesion surrounded by fibrosis.

10. Five patients submitted to surgery for no other reason than for liberation of adhesions.

11. Of the 50 patients, 10 presented granulomas in areas other than the abdomen; 6 cases of granuloma occurred in sinus tracts in which lesions failed to heal following previous surgery; 3 patients presented incisional tumor masses, 1 thought to be a neoplasm; 1 thought to be an incisional hernia (Fig. 4); another a cold abscess. Another patient developed granulomas in the cicatrix of a circumcision, and this necessitated further surgery for marked phimosis.

12. One patient who had previously had a cesarean section presented the interesting combination of dusting powder granulomas and of proved tuberculous peritonitis and salpingitis, the tuberculous and the silicate granulomas coexisting in the same microscopic field.

13. Of the 40 cases presenting abdominal lesions talc granulomas were found in the following sites: in the omentum, 20 times; in the ovary, 18 times; in adhesions, 15 times; in tubes, 9 times; in wall of intestine, 5 times; in serosa appendix, 1 time.

In order, if possible, to determine the quantitative relation between the amount of silicate found and the abundance of the adhesions, the sections and the notes dictated by the surgeon were studied, independently. When 3 granulomas or less per section were found the silicate was termed

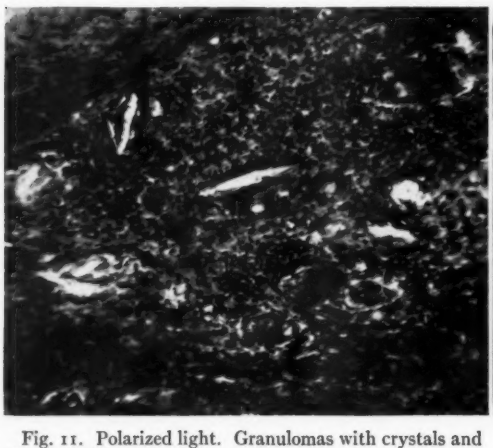


Fig. 11. Polarized light. Granulomas with crystals and giant cells in cortex of the ovary.

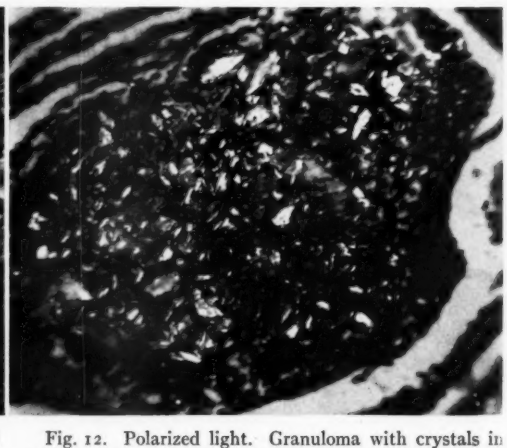


Fig. 12. Polarized light. Granuloma with crystals in rabbit adhesions following traumatization of the serosa.

minimal. When more than 3 granulomas were found per section the amount of silicate was termed abundant.

When the surgical notes mentioned adhesions without description or referred to them as a few, or occasional, the adhesions were termed minimal. When the surgical notes described adhesions as massive, abundant, extensive or in other terms denoting large quantity the term abundant was used. Thus there are four relationships between quantity of silicate and adhesions:

	Cases
Granulomas abundant—adhesions abundant	20
Granulomas minimal—adhesions minimal	8
Granulomas minimal—adhesions abundant	9
Granulomas abundant—adhesions minimal	4

Thus it will be seen that while there are exceptions each way, there is a general agreement as to the volume of the silicate and the quantity of adhesions.

It is true that this is but a crude approximation and many objections may be raised against the conclusion that the amount of adhesions is in direct relation to the amount of talc.

It may be rightly argued that:

1. The case records give no idea as to the extent of the original pathological changes and the peritoneal involvement by those changes.

2. The records give little idea as to the extent of the previous surgery and the traumatization necessitated by that surgery.

3. They give no idea as to the peritoneal manipulation and traumatization produced by the operator (it is admitted that there is a wide difference among surgeons as to the gentleness or roughness of their manipulation of peritoneal covered viscera).

4. Some surgeons make a practice of passing the gloved hands through a sterile hand bath to remove excess dusting powder before operating; others plunge their dry talc covered gloves into the moist peritoneum with no such precaution; others use the wet glove technique, without the use of a dusting powder.

In short, there are too many scarcely appraisable factors to permit a definite conclusion that the quantity of adhesions is directly proportional to the quantity of dusting powder or that the dusting powder is responsible for the adhesions.

In the production of adhesions two things are necessary: first, some form of trauma to the serosa and, second, exudation of fibrin. Although talc granulomas were found in the adhesions as well as beneath the serosa of the viscera, there was no direct evidence that the talc by itself produced the adhesions.

The previous conditions for which the patients were operated upon and the surgery itself would supply both factors necessary for the adhesions.

If the talc can admittedly produce marked reaction in tissues, then what is the relation, if any, of the talc to the adhesions and what is its fate in the tissues?

In an attempt to answer these questions the following animal experiments were carried out.

GRANULOMAS PRODUCED EXPERIMENTALLY

Experiment 1. Intraperitoneal injection talc suspension. Six guinea pigs received by intraperitoneal injection 5 cubic centimeters of a sterile 0.5 per cent suspension of surgical talc in physiological salt solution. The animals manifested no symptoms after the injection.

The animals were sacrificed in pairs at weekly intervals. The intra-abdominal findings were essentially the same, regardless of when autopsy was made. There were no adhesions. Minute yellowish granulomas were visible in the peritoneum of the intestines, in the omentum, and beneath the peritoneum of the fat which is present in the lower abdomen.

Histologically the granulomas consisted of proliferated histiocytes, macrophages, and giant cells with the accumulation of a few lymphocytes. When viewed with polarized light, many silicate crystals could be seen, some in the giant cells, some lying between macrophages and histiocytes. The lesions were covered by an intact layer of peritoneum and upon the surface there was no exudate. The foreign body material had all been buried beneath the peritoneum and surrounded as any inert foreign body. None of the injected material was found free in the peritoneal cavity. The entire process had been completed within 1 week after the inoculation.

For control purposes 1 guinea pig received intraperitoneally by needle 5 cubic centimeters of sterile physiological salt solution. This animal was sacrificed at the end of 3 weeks. The abdominal cavity on autopsy was entirely normal as might be supposed. There were no adhesions. The same saline solution was used throughout all the experiments.

Experiment 2. Intraperitoneal injection talc suspension. Two normal female rabbits received, by intraperitoneal injection and by aseptic technique, 10 cubic centimeters of a 0.1 per cent sterile talc suspension in physiological salt solution. The inoculation produced no manifest symptoms.

At the end of 4 weeks the animals were sacrificed (chloroform) and autopsy was performed. The abdominal cavity showed no increase in fluid. There were no adhesions. A few yellowish granulomas were seen on the large intestine, largely in the mesenteric, not the free, side; a few granulomas were seen in the omentum. There were no other abnormalities.

Histological examination showed foreign body granulomas, consisting of proliferated histiocytes, macrophages, and giant cells. Polarized light demonstrated in the granulomas varying numbers of silicate crystals. The overlying peritoneum was intact and there was no exudate. The talc had been completely removed from the peritoneal cavity and had been immobilized beneath an intact layer of serosal cells.

Experiment 3. Intraperitoneal injection talc suspension, early reaction. In order to study the early reaction of the peritoneum to talc, 2 rabbits were inoculated intraperitoneally with 10 cubic centimeters of sterile 0.1 per cent talc suspension in physiological saline.

The first of these rabbits was sacrificed at the end of 18 hours. At autopsy the peritoneal cavity contained an estimated 3 cubic centimeters of definitely cloudy fluid, slightly yellow in color. About 1 cubic centimeter was pipetted off into a small tube and allowed to stand at room temperature. No coagulum formed at the end of 1 hour. The abdomen showed no macroscopic evidence of inflammation. A few minute whitish flecks were attached to the peritoneal surface and these could not be wiped off. They were obvious aggregations of talc. Specimens from these areas were taken for histological examination.

The fluid removed by pipette was examined cytologically, supravital stain (Ehrlich's neutral red and Janus green) being used. The following cellular elements identified are listed in order: monocytes, large numbers; macrophages, numerous; lymphocytes, few; serosal cells, occasional; polymorphonuclears, occasional.

One or 2 macrophages contained some minute crystals. A few free crystals were seen but care must be exercised in recording free crystals in a hospital where talc is so abundant in the air and upon glassware, however scrupulous the technique.

Autopsy was done on the second rabbit at the end of 24 hours. The findings practically duplicated those in the first. The cellular response in the peritoneal fluid was essentially the same. All the talc had been immobilized and there was none free in the fluid. There were no adhesions.

The character of the cells found in the fluid, the almost complete absence of polynuclears and the absence of fibrin bespeak the nonirritant quality of the talc.

Histological examination of the peritoneal plaques found in these 2 rabbits showed a series of changes in the peritoneum which may be described briefly as follows: When the silicate crystal makes contact with the serosal surface, the serosal cells in the immediate vicinity lose their flat appearance, become globoid, and begin to proliferate. Very soon the crystal is seen lying in a cup composed of these cells. This cup-like mass is elevated above the surface of the surrounding normal serosa (Fig. 5).

The cup is rapidly closed across the top by proliferating serosal cells which completely cover the crystal (Fig. 6). As the process goes on there is a proliferation of histiocytes in the deeper layers in the vicinity. A few monocytes and macrophages appear, the beginning of a granuloma. Very soon the young granuloma instead of projecting above the surface (Fig. 7) comes to occupy a position in which there is little if any alteration of the serosal plane and lies definitely beneath the surface, covered by an intact, smooth layer of serosal cells (Fig. 8). The crystals now usually lie, especially if single, in such a way that their long axes are parallel with the serosal surface.

During the process no exudate of fibrin is seen.

As the granuloma develops giant cells are seen and the crystals may be demonstrated within the cytoplasm of these cells or lying in the interstices between epithelioid cells (Figs. 9, 10).

In some organs, especially the human ovary, the granulomas may be seen at a considerable distance, often as much as a millimeter or more, beneath the surface (Fig. 11).

In the mechanism of the formation of adhesions it is well known that fibrin plays an important part. The inability of silica, *per se*, to induce an exudation of fibrin would suggest that it is not important in the formation of adhesions. These observations would point to a very efficient mechanism of disposal of talc by the peritoneum.

Experiment 4. Laparotomy, no trauma, talc suspension. Two normal rabbits were selected. With aseptic technique, under intravenous nembutal anesthesia reinforced by ether the abdominal cavity was entered through a midline incision; 10 cubic centimeters of sterile 0.1 per cent talc suspension was introduced into the abdominal cavity. The contents of the cavity were left untouched and the incision was closed with two layers of sutures.

At the end of 4 weeks autopsy was performed upon the rabbits. The incisions were well healed without evidence of infection. One rabbit showed some adhesions between the large intestine and the anterior abdominal wall at the site of the incision. Neither rabbit showed any generalized adhesions. A few minute, yellowish granulomas were seen in the peritoneum and in the omentum.

Histological examination showed typical talc granulomas, covered by an intact layer of serosal cells.

For control purposes under aseptic technique and with intravenous nembutal anesthesia reinforced by ether, the abdomen of a third rabbit was opened and 10 cubic centimeters of sterile physiological saline was introduced without disturbing the contents of the abdomen. The abdomen was closed with two layers of sutures. At autopsy at the end of 4 weeks this rabbit showed no generalized adhesions, and there was no evidence of any abnormality of the viscera or the peritoneum.

Experiment 5. Laparotomy, no trauma, dry talc. Under aseptic technique and with intravenous nembutal anesthesia supplemented with ether, the abdomens of 2 rabbits were opened through a midline incision.

Without disturbing the contents of the abdomen some sterile dry talc was dusted on the coils of the intestine. The abdomens were closed with two layers of sutures.

The rabbits were examined post mortem at the end of 6 weeks. A small pyogenic abscess was found in the lower end of the incision in one of the rabbits. This lay external to the peritoneum and had no communication with the peritoneal cavity. There were no generalized adhesions in either rabbit. Numerous yellowish granulomas were found in the peritoneum of the large intestine, the omentum, and in the flanks in the region of the extremities of the oviducts and ovaries. The granulomas were larger than those found in the animals of experiment 4. This probably could be accounted for by both the uneven distribution of the powder, its adherence to moist surfaces, and its consequent slower dissemination throughout the abdominal cavity.

Histologically the granulomas were larger, and contained great masses of crystals. The lesions as usual were covered by an intact layer of serosal cells without adhesions and without exudate. No other control animals were used in this experiment.

Experiment 6. Laparotomy, oophorectomy, traumatization and talc suspension. With aseptic technique and under intravenous nembutal anesthesia reinforced by ether, the abdomens of 2 rabbits were opened through a midline incision. A unilateral oophorectomy was done on both rabbits and the peritoneum of the small intestine of each was vigorously rubbed with sterile dry gauze, to traumatize superficially the serosa. In addition, the serosa was superficially scarified with the scalpel. One hundred cubic centimeters of 0.1 per cent sterile talc suspension was introduced into the peritoneal cavity of one rabbit and the abdomen was closed with two layers of sutures.

For control purposes the abdomen of the other rabbit was closed without the addition of the talc suspension.

Autopsy on both rabbits was performed at the end of 6 weeks. Both rabbits showed adhesions between the small intestine and the anterior abdominal wall at the site of the incision. So far as could be determined macroscopically the adhesions were no more abundant in the talc treated rab-

bit than in the control animal. Had the experiment been allowed to run 6 months instead of 6 weeks it is possible that a difference might have been noted.

Histological examination of specimen from rabbit No. 1 showed subserosal microgranulomas in the peritoneum of the small intestine, in the organizing adhesions in the vicinity of the incision, in the region of the oophorectomy, and in the omentum.

Histological sections from rabbit No. 2 showed no differences other than the absence of granulomas. In the case of rabbit No. 1 the granulomas contributed to an increased bulk of tissue reaction and a repair process.

Experiment 7. Laparotomy, oophorectomy, traumatization, dry talc. With aseptic technique and under intravenous nembutal anesthesia reinforced by ether the abdomens of 2 normal female rabbits were opened. A unilateral right oophorectomy was done on both animals. The peritoneum of the small intestine of each was rubbed vigorously with dry sterile gauze and superficially scarified by the scalpel. Upon the peritoneum of one animal (No. 1) sterile dry talc was dusted. The abdomen was closed with two layers of sutures. The other rabbit (No. 2) was closed without the introduction of talc. The amount of peritoneal trauma was about the same in both rabbits.

At the end of 3 months autopsy was done on both rabbits.

Rabbit No. 1 showed adhesions between the small intestine and the anterior wall at the site of the incision, between the coils of the small intestine, in the region of the oophorectomy, and between the right horn of the uterus and the incision area. Definite yellowish white granulomas were seen in the adhesions (Fig. 12) in the omentum, in the fat in the region of the oophorectomy, and in a few places in the peritoneum of the free large intestine.

Histological examination of specimens showed bulky granulomas in the regions mentioned, including the adhesive bands which united the bowel to the anterior abdominal wall. Elsewhere the granulomas were covered by an intact layer of serosal cells, without adhesions. Rabbit No. 2 showed adhesions between the bowel and the anterior abdominal wall at the site of the incision, between the coils of the small intestine.

SUMMARY AND CONCLUSIONS

Studies have been carried out to determine the response of tissues to surgical dusting powder and to determine the relation, if any, of dusting powder to adhesions and to other lesions.

These studies would indicate that:

1. Talc, although chemically inert, promptly induces a marked tissue reaction in the form of foreign body granulomas.

2. The talc, once immobilized in the granulomas, remains permanently in the tissues.

3. This process is an attempt to immobilize the crystals and is a protective mechanism.

4. This protective mechanism may interfere with normal healing processes depending on the site and the abundance of the granulomas which are present.

5. Talc, *per se*, in the abdomen, in the absence of injury to the peritoneum, is quickly removed from the peritoneal cavity, immobilized and covered by serosal cells, without the formation of an exudate and without adhesions.

6. Adhesions do not develop without some form of traumatization of the peritoneum sufficient to produce exudation of fibrin.

7. Even in the presence of peritoneal trauma and exudation of fibrin, the talc plays a secondary rôle, in that it is caught up in the fibrin and is incorporated in the adhesions. Thus the developing granulomas may either add to the bulk and density of the developing adhesions or may impede the resolution of any adhesions once formed. In this sense it may be said to contribute to the disability produced by adhesions resulting from surgical operations.

In surgery we go to great lengths to exclude one type of foreign body—bacteria. Concerning bacteria it may be said that they can be destroyed by the body and that their removal is complete. It is true that they are capable of reproducing themselves. But for dusting powder, it may be said that although it cannot reproduce itself, it is a completely inert foreign body, incapable of destruction or removal and yet capable of producing local tissue reactions. Its reduction to a negligible minimum could be easily achieved by simple precautions.

REFERENCES

1. Antopol, William. Arch. Path., 1933, 16: 326.
2. Byron, F., and Welch, C. S. Surgery, 1941, 10: 766.
3. Feinberg, Robert. Arch. Path., 1937, 24: 36–42.
4. Gardner, Leroy U. Am. J. Path., 1937, 13: 13.
5. German, W. M. Am. J. Clin. Path., 1940, 10: 245.
6. McCormick and Ramsey. J. Am. M. Ass., 1941, 116: 817.
7. Owen, M. A. Texas J. M., 1936, 32: 482.
8. Ramsey, Thomas L., and Douglas, F. M. J. Internat. Coll. Surgeons, 1940, 3: 3.

EDITORIALS

SURGERY
Gynecology and Obstetrics

FRANKLIN H. MARTIN
Founder and Managing Editor
1905–1935

LOYAL DAVIS, EDITOR

Associates
SUMNER L. KOCH MICHAEL L. MASON

DONALD C. BALFOUR, *Associate, Editorial Staff*

APRIL, 1943

LOBECTOMY, LOBOSTOMY, AND PNEUMONECTOMY IN THE TUBERCULOUS

SINCE the dawn of time man has sought by incision and excision to rid himself of many ills. Each new development in surgery has brought its corresponding attempt to eradicate or alleviate some hitherto hopeless or incurable malady. The problem of surgical removal of all or part of a lung has long intrigued the surgical profession. Recent successful results of lobectomy and pneumonectomy in bronchiectasis and bronchiogenic carcinoma have intensified a desire to apply similar methods to the treatment of selected cases of pulmonary tuberculosis.

Fundamentally this problem in the tuberculous patient differs considerably from that encountered in patients with other conditions. Tuberculosis is a constitutional, not a local, disease. The symptom-producing, clinical lesion is almost invariably a secondary metastatic focus not the primary site of the process. It cannot be eradicated completely by any known means, hence surgery alone cannot cure it. The disease itself may be flared up or disseminated by aspiration, by anesthetic trauma, by surgical manipulation, or by anything which lowers the patient's general resistance. Because of these possibilities, end-results of any type of treatment cannot be accurately evaluated in short periods of time.

Pulmonary tuberculosis of a degree sufficient to indicate, and of a type suitable for treatment by, collapse therapy responds well to pneumothorax, thoracoplasty, and other accepted collapse measures. Four persistent complications, tracheobronchial tuberculosis with stenosis, bronchiectasis, bronchial obstruction with secondary sepsis, and persistent cavity unclosed by all collapse therapy measures, suggest a possible consideration of more radical surgical measures such as lobostomy, lobectomy, or total pneumonectomy.

Lobostomy[1], or external drainage of a lobe of the lung, usually by the Graham cautery technique, is not to be considered for ordinary bronchiectasis or uncollapsed cavity. Its limited field of usefulness lies in relieving the sepsis from an obstructed, infected lung distal to a high grade bronchial obstruction in a patient too ill for lobectomy or pneumonectomy. The symptomatic response is often dramatic. The postoperative care is exacting and prolonged. External healing is slow but may be complete. Extrapleural thoracoplasty to control the remaining disease must follow when conditions permit.

Lobectomy by primary ligation rather than a tourniquet technique may be considered for bronchiectasis or residual uncollapsed cavita-

[1]Some experiences with pneumonectomy, lobectomy and lobostomy in tuberculous individuals. Tr. West. Surg. Ass., 1941, pp. 497–521.

tion. Mobilization may be difficult due to dense scar tissue or matted nodes, and tuberculous tissue may be encountered at any point. Healing of tuberculous tissue may be insecure, and empyema, bronchial fistula, and sinuses may develop. Overexpansion of the remaining lobe after operation may induce an exacerbation of residual tuberculosis. Pneumonectomy rather than lobectomy may be a wiser choice under such circumstances. Extrapleural thoracoplasty before or after the lobectomy may be desirable or necessary.

Pneumonectomy by primary dissection may be considered for residual cavity, for bronchial stenosis, or for bronchiectasis. The contralateral lung should be uninvolved. The main bronchus must be free of disease. Matted mediastinal lymph nodes and dense fibrous tissue may complicate the dissection. Tuberculosis in the pleura or in the tissue sectioned and sutured may result in poor healing, fistula, and empyema. Thoracoplasty later to obliterate the pleural cavity is often necessary.

Procedures of the types mentioned, whether for tuberculous or nontuberculous disease, can be carried out in the tuberculous only at considerably greater risk than in nontuberculous individuals, yet special conditions may, though rarely, justify the attempt. Tuberculosis itself presents the real hazard, with reactivation, dissemination, and poor healing accounting for much of the added risk. Dissection through tuberculous tissue, contamination with tubercle bacilli, and mass ligation leaving tuberculous material in the stump may be expected to lead to trouble. Surgery without adequate preoperative and postoperative constitutional treatment may well prove futile. The development of some new chemotherapeutic agent capable of inhibiting the activity of Mycobacterium tuberculosis for at least 2 or 3 months would prove of inestimable value and permit us to offer relief to a considerable number of patients who are now beyond the reach of surgical aid.

THOMAS J. KINSELLA.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

DURING the past few decades—a period marked by striking advances in all types of surgery performed upon practically every organ and structure of the human body—surgery pertaining to the pancreas has been hampered, in fact practically prevented, by a general edict concerning the dangers of a complicating acute pancreatic necrosis. It was quite definitely stated that if bleeding, necrosis of tissue, or infection resulted from the operative procedure a fatal pancreatic necrosis would likely ensue. This theory or postulation was formulated by physiologists and other experimental workers and so forcibly impressed upon the clinical surgeon that he dared not disobey the mandate for fear of just criticism. In spite of this precept it had been shown by Senn and other clinical surgeons many years ago that operations performed upon the pancreas did not necessarily lead to disastrous results. To be fair to all concerned it must be conceded that surgical technique during the past decade or two has been improved in many details, such as in the gentle handling of tissues, meticulous care in hemostasis, less mass ligation in the control of bleeding, the use of silk for ligating vessels and the like. These factors most logically play a major rôle in the successful surgical attack on organs such as the pancreas; moreover, the improvements in the general care of the surgical patient, such as the prevention or correction of dehydration, blood transfusions for anemia, the adjustment of chemical disbalances, malnutrition and forms of avitaminosis and a host of other potential states contributed greatly to safe surgery by lessening postoperative complications.

Great credit must be given to Whipple for his pioneer work in pancreatic surgery. It is due to his keen judgment, operative skill and courage that pancreatic surgery received a great stimulus during the past decade. Coincident with Whipple's work other surgeons were applying their surgical skill and logical thought to this interesting field of surgery. As a result of this crusade, pancreatic surgery today is being placed upon a sound basis and the pancreas is no longer considered the "ground on which angels fear to tread." The surgeon today is boldly attacking the pancreas, excising tumors and cysts, removing much of the organ when necessary. It has been discovered that many previous deductions as to the need of the external secretion are by no means correct.

Since great strides have been made in the past few years in the relatively new field of pancreatic surgery, there is a definite need for a summary depicting the present status of surgery of the pancreas. Such a monograph has just been prepared by Brunschwig. The author, who is eminently qualified because of his clinical and experimental experiences, has presented a delightful and concise monograph[1] on the surgery of pancreatic tumors. The approach is excellent; concise yet complete; and the material is presented in good literary style. The text is unusually well illustrated, and the greater portion of the illustrations are original.

The text is introduced by a historical chapter. After a consideration of the gross and microscopic anatomy, embryology, and physiology of the pancreas and a summary of the experimental surgery, there are discussed diagnostic procedures, preoperative and postoperative care, pancreatic cysts, cystadenomas, cystadenocarcinomas, benign tumors of the ampulla of Vater, carcinoma of the ampulla with operative treatment, benign tumors of the pancreas, carcinoma of the head of the pancreas and its operative treatment, cancer of the tail and body and its treatment, hyperinsulinism and islet cell tumors and the surgical management, sarcoma, secondary neoplasms of the pancreas, complications of operations upon the pancreas, irradiation therapy of cancer of the pancreas, carcinoma of the pancreas in animals, and experimental pancreatic tumors in animals.

The diagnostic procedures involved in detecting an islet cell tumor associated with hyperinsulinism and the results often obtained with its successful removal form a dramatic episode in modern medicine. This subject is clearly delineated in two chapters. The author has wisely included a consideration of the lesions of the ampulla of Vater because as he states "the problems of their surgical treatment are closely identified with pancreatic surgery."

Concerning carcinoma of the pancreas, there yet remains a note of pessimism that can be observed after a study of the subject. Successful removal requires a relatively wide excision of the tumor from a gross point of view. If the tumor is quite small a wide excision can be done; however, such a small tumor in the pancreas is rarely if ever diagnosed. It is not until the tumor causes symptoms or is palpable that it is detected. By this time it has become adherent to the surrounding structures and in most instances has invaded the surrounding structures or formed distant metastases. Removal at this stage is followed by recurrences. On the contrary, tumors of the ampulla of Vater because of their location cause very early physiological disturbances and can be detected while they may be very small and at a time when no spread or dissemination has taken place. Success should follow in a large percentage of patients who survive the operation.

[1] THE SURGERY OF PANCREATIC TUMORS. By Alexander Brunschwig, M.S., M.D., F.A.C.S. St. Louis: The C. V. Mosby Co., 1942.

This small work is truly one that arouses enthusiasm. There is not a line that does not express some salient fact. It reads like an engrossing story and the illustrations are most instructive. The surgical profession owes a debt of gratitude to the author for this excellent monograph. JOHN A. WOLFER.

CLINICIANS, both internists and surgeons, will welcome the volume on gastric carcinoma by Walters, Gray, Priestley, and their associates of the Mayo Clinic.[1] Backed as it is by a tremendous experience in gastric surgery, it lays particular stress on methods of diagnosis of small and early malignant lesions. A historical introduction is followed by chapters on diagnosis, roentgenology, gastroscopy, special laboratory observations, physiological considerations, indications for treatment, pathological considerations, preoperative treatment, anesthesia, a detailed discussion of the various technical procedures, prognosis, end-results, and statistical data.

Rightfully so, considerable space is devoted to the diagnosis of early lesions and other differential diagnoses of doubtful lesions in chapters on x-ray, gastroscopy, and clinical diagnosis. Emphasis is laid on the need for early exploration in doubtful lesions that do not promptly respond to medical management and stay healed. Chapters on surgical treatment are written with close attention to technical detail and are excellently and profusely illustrated, as is the text throughout.

While the written text is the product of some fifteen or twenty men, it is all interestingly written and makes good reading. This volume is a complete and up-to-date survey of gastric cancer.

J. R. BUCHBINDER.

THE English author, Bramwell from Manchester, and the American, King from Johns Hopkins, state in the preface to their *The Principles and Practice of Cardiology*[2] that the purpose of their text is to present two views, "clinical observation" as the fundamental viewpoint of the British, and "laboratory methods" as the predominant American issue. They also indicate that the volumes are "impregnated by a strongly personal flavor." On this basis, Dr. Bramwell presents his ideas in the first 238 pages, and Dr. King writes the latter half.

History, physical examination, cardiac pain, heart sounds, are discussed by Dr. Bramwell in the conventional manner. There is a chapter on heart disease and pregnancy and also an interesting chapter on "athlete's heart." His discussion of the pulse and cardiac arrhythmias contain the diagrams, sphygmograms, and electrocardiograms of the current English textbooks, as well as phonocardiograms. The reader may question whether these are English "clinical observations" or laboratory methods.

Dr. King presents the American viewpoint in the manner recommended by the American Heart Association from an etiological aspect, covering the distribution, and the various types of heart disease: congenital, rheumatic, bacterial, syphilitic, hypertensive, and others. He devotes a special chapter to the "senescent heart" which is a somewhat indefinite term, contrary to American idea. In general, his precepts are thoroughly conventional.

The book, or better the two volumes in one book, presents the ideas of a British and an American author. If adverse criticism were to be offered, one might contend that an attempt was made to cover too much material in too few pages, in the ordinary textbook fashion. CHAUNCEY C. MAHER.

IN the second edition of Dr. Wangensteen's outstanding monograph[3] he has enlarged particularly upon diagnosis and treatment, indications for, and technique of, surgical procedures; many illustrations have been added.

The particular points of value, which make this volume a "must" to all students of surgery are its adherence to sound physiological principles, its detailed devotion to pathology, to the diagnosis and recognition of types and locations of obstructions, and above all, the clear recognition of the place and indication for both conservative and operative attack. The author has compiled a voluminous bibliography. His illustrations and photographs of apparatus and surgical technique leave nothing to be desired in this phase of his work.

In part 1 is a lucid and physiologically sound discussion of the sources and effects of distention locally and systemically, of absorption in obstruction, and also of the pathology of strangulation. Part 2 is a detailed discussion of the diagnosis of acute abdominal lesions, methods of recognition of the presence of obstruction, and the differential diagnosis of simple and strangulating obstruction. Part 3 covers treatment and embodies an extensive and detailed description of conservative methods of decompression and operative procedures. There is a comprehensive discussion, complete with illustrations, of standardized bowel operations, including a chapter on closed aseptic resection. Part 4 covers the special obstructions, such as obstructions of congenital origin, foreign bodies, volvulus intussusception, and the like.

The reviewer has had the privilege of expressing his opinion in a review of the first edition of this work. He has carefully read the second. In his candid opinion few monographs in modern surgical literature represent the standard of excellence as set forth in this volume on bowel obstruction.

J. R. BUCHBINDER.

[1] CARCINOMA AND OTHER MALIGNANT LESIONS OF THE STOMACH. By Waltman Walters, B.S., M.D., M.S. in Surgery, D.Sc., F.A.C.S., Howard K. Gray, B.S., M.D., M.S. in Surgery, F.A.C.S., and James T. Priestley, B.A., M.D., M.S. in Experimental Surgery, Ph.D. in Surgery, F.A.C.S. Philadelphia and London: W. B. Saunders Co., 1942.

[2] THE PRINCIPLES AND PRACTICE OF CARDIOLOGY. By Crighton Bramwell, M.A. (Camb.), M.D. (Manch.), F.R.C.P. (Lond.), and John T. King, A.B., Princeton, M.D., Johns Hopkins, F.A.C.R. London: Humphrey Milford (Oxford Univerity Press), 1942.

[3] INTESTINAL OBSTRUCTION; A PHYSIOLOGICAL AND CLINICAL CONSIDERATION WITH EMPHASIS ON THERAPY INCLUDING DESCRIPTION OF OPERATIVE PROCEDURES. By Owen H. Wangensteen, B.A., M.D., Ph.D. 2d ed. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1942.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

A TEXTBOOK OF GYNAECOLOGICAL SURGERY. By Sir Comyns Berkeley, M.A., M.C., M.D. Cantab., F.R.C.P. Lond., F.R.C.S. Eng., M.M.S.A. (Hon.), F.R.C.O.G., and Victor Bonney, M.S., M.D., B.Sc. Lond., F.R.C.S. Eng., F.R.A.C.S., M.R.C.P. Lond. 4th ed. London, New York, Toronto and Melbourne: Cassell & Co., Ltd., 1942.

THE ANTIGONADOTROPIC FACTORY; WITH CONSIDERATION OF THE ANTIHORMONE PROBLEM. By Bernhard Zondek and Felix Sulman. Baltimore: The Williams & Wilkins Co., 1942.

MANUAL OF OXYGEN THERAPY TECHNIQUES; INCLUDING CARBON DIOXIDE, HELIUM, AND WATER VAPOR. By Albert H. Andrews, Jr., M.D. Chicago: The Year Book Publishers, Inc., 1943.

HEALTHY BABIES ARE HAPPY BABIES; A COMPLETE HANDBOOK FOR MODERN MOTHERS. By Josephine Hemenway Kenyon, M.D. 3d ed. Boston: Little, Brown & Co., 1943.

PSYCHOSOMATIC MEDICINE; THE CLINICAL APPLICATION OF PSYCHOPATHOLOGY TO GENERAL MEDICAL PROBLEMS. By Edward Weiss, M.D., and O. Spurgeon English, M.D. Philadelphia and London: W. B. Saunders Co., 1943.

INDIGESTION, ITS DIAGNOSIS AND MANAGEMENT; WITH SPECIAL REFERENCE TO DIET. By Martin E. Rehfuss, M.D. Philadelphia and London: W. B. Saunders Co., 1943.

ORTHOPEDIC SUBJECTS. Prepared and edited by the Subcommittee on Orthopedic Surgery of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Philadelphia and London: W. B. Saunders Co., 1942.

ATLAS OF OVARIAN TUMORS. By Gemma Barzilai, M.D., with a preface by Fred W. Stewart, M.D. New York: Grune & Stratton, 1943.

TRANSACTIONS OF THE SIXTY-THIRD MEETING OF THE AMERICAN SURGICAL ASSOCIATION. Edited by Walter Estell Lee, M.D. Vol. 60. Philadelphia: J. B. Lippincott Co., 1942.

TREATMENT OF FRACTURES. By Guy A. Caldwell, M.D., F.A.C.S. New York and London: Paul B. Hoeber, Inc., 1943.

REPORT OF THE CLINICAL CANCER RESEARCH COMMITTEE OF THE BRITISH EMPIRE CANCER CAMPAIGN. Reprinted from the British Empire Cancer Campaign, 1942.

THE SIGHT SAVER. By C. J. Gerling. New York: Harvest House, 1943.

ENDOSCOPIC PROSTATIC SURGERY. By Roger W. Barnes, M.S., M.D., F.A.C.S. St. Louis: The C. V. Mosby Co., 1943.

FRACTURES OF THE JAWS AND OTHER FACIAL BONES. By Glenn Major, B.S., A.M. (Path.), M.S. (Exper. Surg.), Ph.D. (Surg.), D.D.S., M.D., F.A.C.S., with chapters on Radiographic Technic by Lester M. J. Freedman, B.S., M.D., and War Aspects of Jaw Fractures by Arthur Dick, D.D.S., M.D. St. Louis: The C.V. Mosby Co., 1943.

BRONCHIECTASIS; PATHOGENESIS, PATHOLOGY AND TREATMENT. By James R. Lisa, B.S., M.D., and Milton B. Rosenblatt, B.S., M.D. London, New York, Toronto: Oxford University Press, 1943.

PANCREATIC FUNCTION AND PANCREATIC DISEASE; STUDIED BY MEANS OF SECRETIN. By Henrik O. Lagerlöf, M.D. Translated by Helen D. Frey, with a foreword by Joseph H. Pratt, M.D. New York: The Macmillan Co., 1942.

REGIONAL ANALGESIA FOR INTRA-ABDOMINAL SURGERY; WITH SPECIAL REFERENCE TO AMETHOCAINE HYDROCHLORIDE. By Norman R. James, L.R.C.P. & S. (Ed.), D.A. (R.C.P. & S. Eng.). London: J. & A. Churchill, Ltd., 1943.

RENAL LITHIASIS. By Charles C. Higgins, M.D. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1943.

A SURGEON'S FIGHT TO REBUILD MEN; AN AUTOBIOGRAPHY. By Fred H. Albee, M.D., F.A.C.S., F.I.C.S., with a foreword by Lowell Thomas. New York: E. P. Dutton & Co., Inc., 1943.

POSTURE AND NURSING. By Jessie L. Stevenson, R.N. New York: Joint Orthopedic Nursing Advisory Service of the National Organization for Public Health Nursing and the National League for Nursing Education, 1942.

ORTHOPEDIC CONDITIONS AT BIRTH: NURSING RESPONSIBILITIES. By Jessie L. Stevenson, R.N. New York: Joint Orthopedic Nursing Advisory Service of the National Organization for Public Health Nursing and the National League of Nursing Education, 1943.

ORTHOPEDIC NURSING; CONTENT AND METHOD OF THE TEACHING PROGRAM IN SCHOOLS OF NURSING. By Carmelita Calderwood, R.N. New York: Joint Orthopedic Nursing Advisory Service of the National Organization for Public Health Nursing and the National League of Nursing Education, 1942.

CLINICAL PEDIATRICS. By I. Newton Kugelmass, M.D., Ph.D., Sc.D. London, New York, and Toronto: Oxford University Press, 1943.